The Milbank Memorial Fund

QUARTERLY

CONTENTS

		Page
In This Issue		205
Medical Evaluation of Nutritional Status		
Part IV: Ocular Manifestations of Avitaminosis A, with Especial Consideration of the Detection of Early Changes in Biomicroscopy	*H. D. Kruse, M.D.*	207
Part V: Prevalence of Deficiency Diseases in Their Subclinical Stages	*Dorothy G. Wiehl* and *H. D. Kruse, M.D.*	241
Part VI: Dark Adaptation of High School Students at Different Income Levels	*Eleanor P. Hunt*	252
Hemoglobin Values in Pennsylvania Mass Studies in Human Nutrition	*Pauline Beery Mack; Janice Minerva Smith; Catherine H. Logan;* and *Anne Theresa O'Brien*	282
Contraceptive Service in Three Areas	*Regine K. Stix, M.D.*	304
Annotations		327
Social and Economic Aspects of Swedish Population Movements, 1750-1933	*Clyde V. Kiser*	

Vol. XIX JULY 1941 No. 3

Edited by the Technical Staff

Published quarterly by the MILBANK MEMORIAL FUND, 40 Wall Street, New York, New York. Printed in the U. S. A. Subscription: $1.00 a year

IN THIS ISSUE

As AN essential procedure in the medical evaluation of nutritional status there has been a need for a method of detecting subclinical stages of avitaminosis A. In the fourth paper of the series from the nutrition project in New York City, Dr. H. D. Kruse reports on the "Ocular Manifestations of Avitaminosis A, with Especial Consideration of the Detection of Early Changes by Biomicroscopy." Presenting observations on the changes in the conjunctiva, the site affected earliest in the eye, the paper describes the lesions in various stages of development and severity, from very early to far-advanced. The biomicroscopic examination for the initial and mild conjunctival changes permits detection of subclinical avitaminosis A. It is a simple, convenient, rapid, objective method.

Dietary inquiries have indicated that inadequate intake of vitamin A is one of the more common dietary deficiencies. But evidence of widespread avitaminosis A, as determined from examination of persons, has not previously been presented. The paper presents data on the prevalence of this avitaminosis on a low-income group which bears out the indications from dietary studies. It is also shown that recovery under intensive therapy is complete only after some months.

• • •

Methods for the diagnosis of several nutritional deficiencies in their early or mild stages make it possible now to determine with a high degree of accuracy the prevalence and severity of some of the important deficiency diseases. In a report entitled, "Prevalence of Deficiency Diseases in Their Subclinical Stages," from the cooperative investigation, Medical Evaluation of Nutritional Status, Dorothy G. Wiehl and H. D. Kruse have summarized the results of examinations on about 1,000 persons in New York City. The findings for persons of high and of low economic status are in sharp contrast; and the high prevalence of malnutrition in the low-income groups can leave no doubt as to the need for an intensified and improved effort against this public health problem.

Of the procedures proposed for detecting mild nutritional deficiencies, measurement of dark adaptation to determine the presence of night blindness is one that is receiving widespread attention. In "Dark Adaptation of High School Students at Different Income Levels," Eleanor P. Hunt presents from the cooperative nutrition study in New York City the second article which has described the experience in this Study with the adaptometer developed by Hecht and Shlaer. Visual threshold measurements for students from high and low socio-economic levels are compared; the problem of identifying threshold levels that can be considered unusual is discussed; and the various factors that may be associated with impaired vision under dim illumination are considered.

• • •

Although methods for determining the hemoglobin level of blood are not new, there is surprisingly little information on the prevalence of anemia in general populations. Certainly adequate amounts of iron must be considered as essential to human health as adequate amounts of other food factors. There is need to improve our knowledge of the prevalence of iron deficiency, and the paper on "Hemoglobin Values in Pennsylvania Mass Studies in Human Nutrition" reports the findings from a survey on an unusually large scale. The authors of this report, Pauline Beery Mack, Janice Minerva Smith, Catherine H. Logan, and Anne Theresa O'Brien, suggest that, in spite of the lack of specific hemoglobin standards for adequate or optimal levels, there is unmistakable evidence of cases of poor nutritional status with respect to hemoglobin among persons who are presumably in good health.

• • •

In "Contraceptive Service in Three Areas," the second of two articles appraising birth control services in different sections of the United States, Dr. Regine K. Stix presents data on the experience of the patients after attending clinics in New York City; Cincinnati, Ohio; and Spartanburg, South Carolina.

The policies of all three clinics were similar, and were typical of policies of other contraceptive services. The single type of contraception usually prescribed proved very effective for the patients using it, but the author believes that all services would be more effective if the present policies were modified to meet the special needs of individual patients.

MEDICAL EVALUATION OF NUTRITIONAL STATUS[1]

IV. THE OCULAR MANIFESTATIONS OF AVITAMINOSIS A, WITH ESPECIAL CONSIDERATION OF THE DETECTION OF EARLY CHANGES BY BIOMICROSCOPY

H. D. KRUSE, M.D.

THIS paper, in the series on the medical evaluation of nutritional status with emphasis on the recognition of early impairment, presents a preliminary report of observations on ocular changes in avitaminosis A as seen in the gross and with the biomicroscope, and particularly the biomicroscopic examination of the conjunctiva as a means of detecting early avitaminosis A.

When manifest ocular lesions of avitaminosis A were observed in a considerable number of persons in an adult group, the eye examination not only in the gross but also by biomicroscope was extended to the entire group. The principal manifestation was xerosis conjunctivae, often with mild xerosis corneae. The cases could be arranged in three main categories. In some there were gross ocular manifestations in the form of characteristic elevated spots, the so-called Bitot's spots, a feature of advanced xerosis conjunctivae. Others showed less pronounced but unmistakable gross conjunctival changes without a spot; but much more by biomicroscope. Finally, some exhibiting very little if anything grossly, showed definite changes only by biomicroscope. The number of cases was sufficiently large to show all lesions as various stages in one process.

Following administration of vitamin A as specific therapy, the conjunctival lesions in nine persons have now completely disappeared, as judged by microscopic examination. In all others receiv-

[1] This paper is the fourth of a series from a cooperative investigation by the United States Public Health Service, Division of Public Health Methods; the New York City Department of Health; the Cornell University Medical College, Department of Public Health and Preventive Medicine and Department of Pediatrics; and the Milbank Memorial Fund. Reprinted from United States *Public Health Reports*, June 27, 1941, 56, No. 26, pp. 1301-24.

The cooperating agencies have been assisted in carrying out this investigation by the Work Projects Administration for the City of New York, Official Project No. 65-1-97-21, W.P. 24, "Medical Evaluation of Nutritional Status."

ing therapy, the conjunctival lesions have markedly receded, in many to the point of near disappearance. Those not receiving therapy have shown no improvement.

Description of Group and Procedures

One hundred and sixty-six adults, 17 to 65 years of age were examined for grossly elevated spots. Forty-five were white females; seven, colored females; 107, white males; and seven, colored males. The white individuals were from various racial stock. None regarded themselves as sick, and all attended work regularly. All except three received incomes ranging from $52-95 a month.

Their eyes were examined prior to therapy. Twenty-three persons permitted only gross examination, but are included in the total for calculation of the proportion of gross spot cases. The others were examined with the biomicroscope as well as in the gross. Both types of examination were limited to the area of the bulbus exposed upon extreme rotation in many directions. In addition, the inside of the lower lid of some individuals was examined grossly, but the upper lid was not everted.

Inasmuch as specific skin lesions have been reported as an early manifestation of avitaminosis A, the skin was examined in forty-seven persons with all grades of severity of ocular lesions prior to vitamin therapy. Solely for convenience, the skin examination was restricted to males among those listed for therapy. A brief history of ocular symptoms was likewise taken from these same individuals.

For ascertaining the dietary requirements of vitamin A, dietary records were taken from a selected number representative of the various stages of the conjunctival lesion, as well as those not showing it. On most of the persons with lesions, adaptometer tests were conducted before, at various intervals during, and upon completion of therapy. The results on requirements and the correlation of conjunctival lesions with dark adaptation will appear in subsequent papers.

Because of the gravity of advanced conjunctival changes, all persons with fully developed, elevated Bitot's spots were offered, even urged, to take therapy. A few refused for various reasons; they thus formed a control group for the advanced cases with spots.

Of those individuals showing gross conjunctival changes without spots and those showing only microscopic changes, only a part received therapy. Cases were graded by severity into groups from which individuals to whom therapy was offered were selected at random so that twenty-three of seventy-eight persons received therapy.

Therapy was instituted in one group on September 23 and in a second group on November 1, 1940, and consisted of 100,000 U.S.P. (International) units of pure vitamin A in four capsules of 25,000 units each during the day. For the most part, the therapy was taken in the presence of the dispenser, during the five work days; for over the week-end a supply was given to be taken home. None of the individuals were advised of the nature of their ocular condition and its probable dietary basis. No change in diet was advised, in order that there would be no suggestion or encouragement to take other or additional supplements *ex cathedra,* or to modify dietary habits.

A very few among those receiving therapy, as well as those not receiving therapy, have since become unavailable through departure and could not be further followed. Through some whim, one or two stopped therapy. In all, sixty-one persons are still receiving vitamin A capsules; treatment has been discontinued on the nine now completely restored. Eye examinations have been conducted at intervals on the groups receiving and not receiving treatment; for the former these examinations have formed the basis for terminating therapy.

Ocular Signs and Lesions in Gross "Spot" Cases

Of the one hundred and sixty-six persons examined, sixty-five (39 per cent) had one or more manifest spots.

For the most part, the manifest spot cases include the most advanced cases. By manifest spots is meant grossly perceptible elevated conjunctival spots of distinctive color and characteristic location. Since these patients exhibited different phases of the advanced stage, the observations, both gross and microscopic, are most lucidly and succinctly presented by a composite description. (Figures 1 and 2. These are described on pages 239 and 240.)

Facing bright daylight but not sunlight, most "spot" cases showed definite photophobia and lacrimation most readily elicited, however, upon examination with the slit lamp. Almost all of these patients had previously been aware of these disturbances, but it is striking that so few had noticed the spots until called to their attention.

The caruncle and plica semilunaris were usually swollen and engorged. In many instances the eyelids were swollen. The inferior fornix conjunctivae showed looseness, additional folds, and some congestion.

The vascular network in the conjunctiva was conspicuous; vessels converged radially from the canthus and fornices towards the limbus. These are large, prominent, superficial vessels from which, by close inspection, numerous lesser branches may be seen to ramify and form a fine network. This vascular pattern is distinct, but what at first seems paradoxical, the vascular plexus appears less pronounced and extensive in the eyes with most severe conjunctival involvement. Often in these instances the large vessels seem to reach only half way to the limbus.

Generalized changes varying with severity occurred in the bulbar conjunctiva. In bold outline one part may be elevated in bandlike form above the remaining conjunctiva. There is usually wrinkling or folds, frequently along the line of apposition of the bulbar with the upper margin of the lower palpebrum, although vertical crescentic folds are sometimes seen near the inner canthus. In detail the surface shows further unevenness because the conjunctiva is raised

slightly over the vessels, leaving small shallow depressions in honeycomb pattern within the vascular outlines.

In texture the conjunctival surface may be smooth or rough; invariably it has diminished luster. Its color may be creamy, ivory, white, greenish-white, whitish-green, or bluish-milky, according to severity. Very frequently it is a yellowish orange, taupe, or gray brown with underlying whitish green, due to association with vascularization. In appropriate light the conjunctiva of the partially advanced cases showed opalescence; sometimes it was greenish yellow, sometimes amethyst, but most often it had a silvery or galena hue.

Moreover, in seven cases pigmentation was seen as sharply localized deposits or as a narrow rim following the boundary of the limbus. This occurred only in the colored individuals, never in the white.

Depending on the stage of severity, the conjunctiva showed changes in its transmission of light. In the most advanced cases, it was opaque. The color of the choroid shining through the sclera, indeed most of the vascular network, was completely obscured. Where there was opalescence, the conjunctiva was usually translucent. Frequently the superficial strata of an elevated area appeared as a transparent film, much as if a sheet of cellophane were superimposed on an opaque conjunctiva. Less advanced cases showed various degrees of translucence or diminished transparency.

That the conjunctiva is thickened may be inferred from the following gross manifestations: The irregular surface with its bandlike elevations; the very great depth to which light penetrates in the opalescent cases; the thick superficial transparent film.

Uneven contour, diminished smoothness, lackluster, and wrinkling of the surface, opalescence, localized pigmentation, thickness, changed color, and decreased transmission of light all characterize manifest xerosis conjunctivae.

The large series of "spot" cases with lesions in various gradations

of development presented many intermediate stages of xerosis up to fully developed. In one zone of an eye, the changes may occasionally, in advanced stages, be of a similar degree over the entire area, but for the most part they do not occur uniformly. Because of what appears to be predilection in the site of progression, there are various topical patterns of color, thickness, and transmissibility. Frequently in the nasal zone the conjunctival thickening and opacity is limited to the third adjacent to the canthus. At the equator this may converge to a band which runs to the limbus. Thus, in the less advanced cases, the changes may be limited to a localized segment or band, but later they may extend over the entire zone with the band forming a superstructure. The most marked involvement is near both the canthus and limbus.

The Bitot's spot occurred as part of the same process of conjunctival change. It is a small localized area where the tissue change is most advanced. In the first classification of individuals the criterion was arbitrarily adopted that the area must be elevated above its surrounding tissue in order to be regarded as a Bitot's spot. Its more pronounced color and opacity, as well as its elevation, gives it a rather well-defined border and makes it grossly distinguishable from the remaining altered conjunctiva.

Almost always the spot was located at the junction of the equator and limbus. It was most frequently triangular with the base adjacent to the limbus; but other shapes, such as oval, occasionally occurred. Its surface contour was various; flat, undulatory, ridge, and dome forms occurred about equally. In color the spot was usually white, creamy, yellow, or orange, and almost always it was opaque. It varied in the extent to which it was elevated above the rest of the conjunctiva.

Among the large number of persons the spot was observed in various stages of formation; hence, the variability in size, elevation, and color. In general, the white spots were in the earlier stage of development, while the yellow or orange were in the advanced

stage. Just as the spot occurred in various stages of development, it was associated with various stages of change in the rest of the conjunctiva, but the latter was always less advanced. In the spot cases there was no gross opacity in the cornea.

Considering both the entire conjunctival lesion and the spot jointly, the degree and extent of change were usually not the same in the two zones of the same eye. In eleven persons, one spot occurred; in nine persons, three spots occurred. When two eyes were involved, each with one spot in corresponding zones, nasal lesions were more frequent than temporal. Where spots occurred in all four zones, the nasal lesions were usually more advanced than the temporal. Here the similar zones of the individual's two eyes, e.g., the nasal zones of both eyes, often but not invariably showed a like degree and extent of change. The distribution of cases according to number of spots was as follows: one spot, 11 persons; two spots, 31; three spots, 9; and four spots, 14.

Biomicroscopic Examination. Illumination of the eye with the slit lamp brings out clearly any photophobia and lacrimation.

Upon biomicroscopic examination the large superficial conjunctival vessels were seen to ramify into medium-sized vessels which in turn branched into fine vessels; these medium and fine branches of one vessel anastomosed among themselves and with those of another to form the network. If the conjunctiva is translucent, the vessels can be seen at several levels. Furthermore, the superficial vessels anastomose with deep vessels at various points besides the limbus. The superficial network is more extensive than the deep network. If the conjunctiva is opaque, the several strata of the superficial vessels, as well as the deep vessels, are completely obscured. The greater the impenetrability of the conjunctiva to light, the less prominent the vascular network; thus, paradoxically the more advanced stages of the process appear to have less vascular involvement. All the superficial vessels are dilated and engorged, even in the early stages; this accounts for their gross prominence. Such

deep vessels as may be seen are usually likewise dilated and engorged.

In avitaminosis A the vascular reaction at the limbus, while somewhat similar in tendency to that in ariboflavinosis, shows distinct differences. In the "spot" cases the process instead of occurring all around the limbic circumference is limited to two arcs from 8 to 10 and 2 to 4 o'clock. There is no plexiform tiering; the arcades, failing proliferation, do not extend beyond one layer. This single tier of arcades is not continuous, for here and there anastomosis has failed so that there is an interrupted pattern. Thus it appears as a vascular serration with missing teeth. Furthermore, invasion of cornea by the capillaries was slight, negligible, or absent. Corneal opacity was relatively infrequent. This is not to say that in still more severe cases the vascular reaction at limbus might not be more pronounced. In present cases, however, it was less developed and extensive there than that seen in early ariboflavinosis. Although the avitaminosis A was in an advanced stage with its most pronounced conjunctival change adjacent to the limbus, the vascular reaction there was not of the same order. Unlike that in ariboflavinosis, it was most pronounced in the superficial vessels over the conjunctiva.

Besides the vascular reaction in the grossly elevated "spot" cases, the biomicroscope reveals details of changes seen grossly, as well as those not seen grossly. The topography of the conjunctiva (surface contour) is seen to have areas of localized elevation in the form of a band, spot, or both. Wrinkling, observed grossly, is especially prominent under the biomicroscope, and is located at the line of apposition of the superior border of the lower lid with the conjunctiva bulbi. Small conjunctival cysts when situated superficially may produce a bulge, but more often they are situated deeper. Localized pigment deposits as granules or powder may be seen in some cases.

It is convenient to consider the observations on thickness and light transmission in an entire zone, and then in the spot. When part of the conjunctiva is seen to be elevated, increased thickness is

inferred. Elsewhere thickness may be determined through orientation with deep vessels. Where there are several layers of superficial vessels and opacity obscures the deeper superficial as well as the deep vessels, this may be misleading. Then some of the superficial vessels are apt to be mistaken for the deep, and increased thickness may not be recognized. In almost all instances where a spot was present, there was increased thickness of the conjunctiva over most of that zone.

In the biomicroscopic examination of the conjunctiva it is possible to recognize with slit-lamp illumination three main degrees of transmission of light: transparency, translucency, and opacity. Since the conjunctiva was always examined under tension from rotation of the eye, any diminution of transmission was minimized rather than exaggerated. A transparent conjunctiva illuminated diffusely permitted the scleral landmarks and deep vessels to be seen distinctly. Under focal illumination the conjunctiva itself appeared as a moderate suspension of fine flakes in a clear medium. When translucence prevailed, by diffuse illumination the scleral landmarks and deep vessels were seen indistinctly as through frosted glass, or were almost completely obscured. By focal illumination the conjunctiva presented a uniformly dense suspension of opaque flakes in a turbid medium; with the gradations in translucence there was considerable variability in the size of the flakes, the turbidity of the medium, and the density of the suspension. With opacity, the conjunctiva by diffuse illumination was impervious to light and deep vessels were not visible. Here focal illumination added little to recognition.

Transmission of light was frequently not uniform for the entire area of a zone. For example, on the equator at the midpoint there may be punctate opacities which under indirect illumination are shown to be isolated flocculent clumps. Nor was transmission always uniform throughout the depth of the conjunctiva. The superficial layers of the conjunctiva were often more transmissive than

the deep. By diffuse illumination the larger deep vessels were palely outlined as though frost-covered. Thus, the translucence appears to be mainly in the deep conjunctival layer, or, with the upper layer transparent or translucent, the deep vessels—and probably also the deeper rami of the superficial vessels—may be entirely obscured. Here the opacity is restricted to the deep layers with their surface having a cottony appearance.

Accordingly, in classifying the transmissiveness of the conjunctiva with reference to these two strata, the following categories were used: Tr Tl, Tl Tl, Tr O, Tl O, OO. As may be readily recognized, Tr, Tl, and O are abbreviations for transparent, translucent, and opaque, respectively. The first character of the symbol for each category refers to the superficial conjunctival strata; the second character to the deep. It should be cautioned that where the deep conjunctival layers are less transmissive than the superficial—as in TrTl, Tr O, or Tl O—an extensive superficial vascular network may be mistaken for the deep, increased conjunctival thickness may be overlooked, and an erroneous conclusion reached.

In a zone with a spot, all degrees of transmission were observed in the rest of the conjunctiva. As might be expected, when the spot is in the earliest stage of development, there is least change in the remaining area; when the spot is more fully developed, there is general zonal opacity.

The spot itself, as seen microscopically, shows changes more pronounced than elsewhere in the conjunctiva. Viewed by diffuse illumination, it may exhibit scattered dots of opacity; by either focal or indirect illumination these are seen to be due to isolated clumps of flocculent material. When farther advanced, the opaque mass may comprise a dense coalescence of flakes with loose aggregates around its border. Developed still more, the spot may appear either gelatinous or horny.

In a few instances where gross examination revealed a spot characteristic in all respects except that it did not project above the

adjacent surface, it was possible by microscope to confirm its identity and to determine whether it was at all elevated. Then, too, in some zones the microscope detected very early opaque spots which were not grossly perceptible. Actually, both these types are true spots in the very early stages, but they are not included in the foregoing data on the number of persons with spots or on the zonal distribution of spots.

Individuals Without Manifest Spots

The conjunctivae of seventy-eight individuals without manifest spots were also examined grossly and microscopically. Presenting many gradations, the observed changes extended over a wide range. Profound gross alterations were seen throughout some zones, never as advanced as in most severe "spot" cases but definitely more pronounced than in early "spot" cases. The most advanced showed extensively the characteristic color changes, lackluster, and opacity. Gross nonelevated spots were observed occasionally at the junction of the equator and limbus. Some persons exhibited only the characteristic superficial vascular network in the conjunctiva. On the whole, the "nonspot" group showed less intensively any of the characteristic conjunctival changes than did the manifest spot group. Indeed, in the mildest stage little or nothing may be seen grossly; the initial changes may be revealed definitely only by biomicroscopic examination.

In practice it was convenient to classify all the "nonspot" cases according to the severity and extent of involvement on the basis of microscopic findings. Severity was judged by the degree of light transmission with transparency, translucency, and opacity representing progressively advancing stages. Where transmission differed in the superficial and deep conjunctival layers, that in the latter was regarded as decisive. Classification into the three main groups was determined by the most severe state predominating in any one zone. Then subgrouping according to extent was based on

the number of zones showing preponderantly the same condition.

Certain manifestations were noted in association with particular stages. Usually light transmission was in inverse proportion to the thickness of the conjunctiva. The vascular network, as seen microscopically, is least extensive and complex in pattern in the transparent conjunctiva. It appears to be more extensive and elaborate in translucent conjunctivae than in opaque. In opaque conjunctivae the network may seem to be as inconsiderable as in transparent conjunctivae. This is because the opacity obscures most of the network which in actuality is most extensive and elaborate.

In the seventy-eight "nonspot" persons, the microscopic observations on light transmission through the conjunctivae revealed all stages over a broad range. Seventy-seven of them had diminished transmission in one or more zones. Thus, 99 per cent of the "nonspot" group showed definite signs of avitaminosis A. Twelve persons showed only marked translucence in one or two zones. Judged by less strict criteria, which excludes these twelve persons, sixty-five (83 per cent) of the "nonspot" group had marked translucence in three or four zones, or opacity in one or more zones.

Of the 143 persons examined with the biomicroscope, 45 per cent had manifest spots (gross) and another 54 per cent had distinct characteristic microscopic changes. By the method of classification which includes grouping of the "nonspot" cases according to the degree of light transmission, 45 per cent of the persons had one or more spots, 31 per cent had one or more opaque zones, and 23 per cent had one or more markedly translucent zones as determined by microscopic examination. It should be noted that Bitot's spot is merely one stage in manifest xerosis conjunctivae. In some of the "nonspot" group, among a number of those presenting opaque zones upon microscopic examination, the xerosis was of such severity that it was also grossly perceptible.

Changes on Therapy

Upon administration of 100,000 I.U. vitamin A daily to both

"spot" and "nonspot" cases, regardless of severity, the initial changes detectible by microscope were the same. There was diminution of engorgement in the superficial network with vessels still dilated. The circulatory stream did not fill the vessel and its flow was slow; then there was granular circulation followed by beaded or empty vessels. The latter were seen as shadow vessels. With this retardation in flow or disappearance of the stream, the vessels diminished in size. In most instances these vascular changes took place first in that half of the conjunctiva which borders on the cornea. Soon thereafter the entire conjunctiva, which may have been translucent or opaque, became gradually thinner and more transparent. With diminution in thickness of the conjunctiva, cysts and superficial wrinkling are not infrequently seen as transient manifestations. The clearing in the medium advances while recessive changes in vessels are continuing, yet vessels may seem more numerous because many previously obscured by opaque medium now become visible. Gradually the spot diminishes in size, becomes perceptible as an opacity only by microscope, and finally disappears. If the treatment is complete, the conjunctiva becomes smooth, thin, lustrous, much less vascularized, and highly transparent or very slightly translucent.

In persons with gross lesions, several weeks after beginning repair had been followed by microscopic examination, signs could also be recognized by simple inspection. Perhaps the earliest improvement grossly perceptible was in lessened photophobia and lacrimation. Later it was noted that the conjunctiva had changed from opaque white to translucently bluish; at first slight and only in a small area, then gradually increasing in extent and completeness. The decreasing thickness and increasing clarity of the conjunctiva permit the choroid shining through the sclera to be seen. For a time Bitot's spot may appear more prominent because its borders are more sharply outlined and its opacity is cast into sharper contrast by the clearing in the adjacent, somewhat less severely affected conjunctiva. Gradually the spot diminishes in size and disappears. The swelling in the

caruncle and lids recedes. Finally, upon complete recovery, the conjunctiva has a bluish-milk shade and has taken on a noticeable luster and sparkle which enliven the eyes and impart an animated expression to the face.

It should be noted that the criteria of complete recovery are rigorous since they are based on microscopic observations: slight translucency and thinness of the conjunctiva with inactivity in or absence of an excess vascularity. After receiving therapy for eight months, one person with spots has been completely restored and discharged. In all others with spots, the conjunctiva has become less vascular, thinner, clearer, and more lustrous. The spots are much diminished in size; in many no longer grossly elevated; in some detectible only by microscope. Of the persons with "nonspot" lesions, eight have been fully restored and discharged. Naturally, since the "nonspot" lesions are usually less severe, more in this group were among the first to show complete recovery. Nevertheless, they have required not less than six months' intensive therapy.

In both groups those who have not received therapy have shown no improvement.

Following the full recovery of those still receiving therapy, there will be a more complete report.

The results of the adaptometer tests, under rigid conditions of test and with specially calibrated instruments, will be published soon in a preliminary report. At this time it may be said that only a few very high values were found in the total range for the entire group. Not all persons with most advanced xerosis showed high levels, nor were high levels restricted to those with most pronounced xerosis.

Discussion

The ocular manifestations of avitaminosis A are xerosis conjunctiva, including Bitot's spot, and xerosis corneae with subsequent corneal turbidity, ulcer, and keratomalacia. There is a very extensive bibliography dating back over one hundred years on the nomenclature, etiology, and pathogenesis of the conjunctival and corneal

changes, as well as their interrelation, but its presentation will be reserved for a later paper. Yet it is worth while to mention here that all these manifestations in the order enumerated are regarded as successive stages of one process.

Since the present study pertains only to the initial stages, it is appropriate to cite briefly some of the original observations on the conjunctival lesions. Although the first description is usually attributed to Bitot (4) in 1863, Cohn (5) cites sixty prior references to the condition dating back to 1803.

During this time it was known by various names. Some of these, such as xerophthalmos (6), xeroma (7), conjunctiva arida (8), and dry conjunctiva (9), expressed the dryness so often present in the pronounced stage.

Several authors preferred to stress the primary nature of the lesion. Accordingly, from its histogenic character, they denoted it under the descriptive names of cuticular conjunctiva (10), Ueberhäutung der Conjunctiva (11), Hautbildung der Bindehaut (12), skinning over the conjunctiva (9). These terms are highly expressive of its histogenic nature and gross appearance, what is today called the metaplastic character of the epithelium.

Then von Ammon (13), more concerned with differentiating its etiological independence of an inflammatory process than in denoting its essential character, proposed the name of xerosis conjunctivae. In a footnote, he explained: "Xerosis (η ξηρωσῖς), das Trocknen, Austrocknen. Der Herausgeber hofft, dass dieser Name durch die Beschreibung und Charakterisirung der Krankheit sich rechtfertigen wird. Er hat die bekannteren Wörter, Xerophthalmos oder Xeromma (v. ξηρος und ὄμμα), deshalb nicht gewählt, weil die Grichen, da, wo sie dieses Wort gebrauchen, hiermit die in Folge der Entzündung der Bindehaut oder anderer Theile des Auges entstehende Trockenheit dieses Organs bezeichneten." But the choice was not fortunate inasmuch as it was still vague and misleading.

Later Bitot (4) described the conjunctival lesions as epithelial strata or plaques assuming various shapes, but he gave them no name. Subsequent to his publications, several of his contemporaries referred to them as Bitot's spots, a name which has since gained some currency.

At the present time there is no satisfactory nomenclature expressing the true nature of the lesion. Unfortunately, it still retains the designations xerophthalmia and xerosis conjunctivae which are open to misconception because dryness is not its primary or most significant characteristic and is recognizable only in pronounced cases. Moreover, xerophthalmia is not specific for the conjunctival stage since it includes xerosis corneae as well as xerosis conjunctivae.

To some extent Bitot's spots are mentioned in the literature, but such an eponymic designation is not to be recommended. Besides, it applies only to a very particular stage of the conjunctival lesion. Of the three terms still in vogue, xerosis conjunctivae is perhaps the least objectionable to denote the conjunctival lesion, but it should carry a connotation of the fundamental nature of the lesion.

Xerosis conjunctiva, and the more advanced stage xerosis corneae, were reported in association with a series of diseases and were attributed to numerous causes. Within two years of Bitot's observation, Gama Lobo (14) asserted that xerosis occurring in Brazilian slaves resulted from lack of suitable and sufficient food. In the next year Blessig (15) noted that the xerosis appeared preponderantly during the seven-week Lenten fast and receded thereafter. He insisted that it was the consequence of a nutritional disturbance which was not simple inanition, and suggested lack of nitrogenous substances. Calling attention to the severe disturbance of the general nutritive condition so frequently observed with the eye lesions, Förster (16) in 1877 inclined to the view that "nutritive deficiency" was responsible for the ocular changes, comparable to such trophic disturbances as decubitus and diabetic gangrene. Shortly thereafter de Gouvêa (17) declared that xerophthalmia is a natural conse-

quence of the general nutritional disturbance caused by chronic progressive anemia which resulted in part from heavy labor and an insufficient and deficient diet. In the same year Thalberg (18) reported the occurrence of keratomalacia in infants nursed by mothers who gave sufficient milk but were anemic or debilitated by prolonged fasting. Likewise, Schoeler (19) in 1887 observed the ocular lesions in adults who were on restricted or unbalanced diets.

From 1866 to 1904, twelve reports appeared on the successful use of liver or cod-liver oil internally for xerophthalmia (20). In treating more than 1,500 infants with xerosis conjunctivae, Mori (1904) (21) found immediate and specific response to cod-liver oil. Since their diets contained little fat, and they responded to liver oil, he attributed the ocular lesions to inadequate fat. He advanced this hypothesis despite his lack of success with sesame or olive oil.

In 1906 Falta and Noeggerath (22), feeding rats on a "purified" diet, noted the development of a conjunctivitis in the course of their general nutritive decline. Reproducing these results in a further investigation of this possible relationship between the conjunctival disease and diet, Knapp (23) in 1909 drew the interesting conclusion that the eye disorder was due to a specific dietary deficiency of an unknown substance. Then came McCollum and Davis' (24) demonstration that growth was not possible in rats restricted to a standard ration unless a substance contained only in certain fats (fat-soluble A) was included. Shortly, Osborne and Mendel (25, 26) pointed out that inflamed and purulent eyes appeared in animals on diets deficient in the fat-soluble vitamin, one source being cod-liver oil, and disappeared upon administration of it.

Whereas the preceding observations revealed a deficiency of fat-soluble A as the cause of an eye disease, but did not identify the latter with xerophthalmia; other investigations next showed that the ocular disease induced experimentally by a deficient diet was really xerophthalmia, but did not recognize and identify the missing dietary factor as fat-soluble A. Using a diet complete in calories and

known constituents but deficient, as they knew, in certain other unidentified indispensable substances, Freise, Goldschmidt, and Frank (27, 28) asserted that they had experimentally produced keratomalacia. They placed it among the deficiency diseases, but their experiments did not permit them to characterize the deficiency.

Impressed by the low fat content in the diets of his xerophthalmic patients and the striking efficacy of cod-liver oil in an epidemic in Denmark during World War I, Bloch (29), though cognizant of McCollum's results, subscribed to Mori's theory of fat deficiency as the cause of the eye disorder. McCollum and Simmonds (30) thereupon enunciated the view that xerophthalmia in human beings and in rats was analogous, representing a deficiency in vitamin A. They said: "We feel confident that these cases of xerophthalmia reported by Mori and Bloch should be looked upon as a 'deficiency disease' not hitherto recognized in its true relation to diet. It is not, as these authors believe, a 'fat starvation' which produced the condition, but a lack of the unidentified dietary factor, fat-soluble A, which occurs in just those foodstuffs which they observed to possess curative properties."

Night blindness is another ocular manifestation reported as appearing in avitaminosis A. Literally it is failure or imperfection of vision at night or in dim light. There is an older and more extensive recorded history for night blindness than for xerosis. Among the views on its etiology, the nutritional was based on dietary inquiries or observations on effective therapeutic agents.

In old Chinese medicine, chicken or sheep liver was highly recommended as a specific for night blindness; and among the home remedies, chicken-liver extract in honey was popular (31, 32). In 1859 Graefe (33) designated insufficient and poor food as a contributory factor in its causation. Following Bitot's contention that xerosis and night blindness were associated as parts of the same process, it might be expected that both would be attributed to the same cause and that therapy found effective for one would be used

for the other. But, in the main, developments in views on their cause did not proceed in parallel.

Some of the early investigators who put forward the hypothesis of a nutritional etiology of xerosis did not mention any associated night blindness, nor even suggest that the same cause might be responsible for both (16, 18, 19). On the other hand, several of their contemporaries reporting that night blindness appeared under conditions of poor nutrition, as in prisons (34, 35) and after long fasts (36), presented it as an independent entity. From 1863 to 1910 there appeared a series of reports on the beneficial effects of cod-liver oil or liver for night blindness: in one or two xerosis was mentioned but with skepticism or uncertainty over any relationship to night blindness; in most, xerosis was not mentioned; in some, scurvy was cited as a significant associated manifestation (37, 20). Epidemic night blindness was stated by a few to be a consequence of faulty diet, particularly an imbalance (37); one specified fat deficiency (38).

It is true that Blessig (15) in 1866 charged both xerosis and night blindness to a nutritional disturbance occasioned perhaps by a deficiency of nitrogenous substances. Krienes (37) in 1896 attributed concurrent essential night blindness and xerosis to the same causes, of which one was nutritional disturbance. Groenouw (39) in 1904 mentioned the simultaneous occurrence of the two signs on long voyages where the diet was unsatisfactory. Furthermore, de Gouvêa (17) in 1883 and Mori (21) in 1904 reported that both conditions responded to cod-liver oil. Accordingly they stated that the two manifestations had a common cause; the former suggested improper and insufficient food; the latter specified a fat deficiency. These were clear exceptions to the trend to consider night blindness apart from xerosis.

Even during the period from 1913 to 1917 when vitamin A was discovered, when the occurrence of xerophthalmia in A-deficient animals was observed, and when xerosis in persons was found to be

a manifestation of avitaminosis A, any relationship of night blindness to these developments was not at once demonstrated. Perhaps the reason lies in the course of events peculiar to night blindness. Very early it was reported as occurring alone and also in association with numerous diseases. In classifying its appearance under many circumstances the earliest distinction was between idiopathic or epidemic and symptomatic. In 1881 Parinaud (40) suggested that night blindness is dependent on a disturbance of the visual purple in the retina. Treitel (41) in 1885 concluded that it is characterized essentially by a disturbance in dark adaptation. In turn, this was attributed to involvement of the visual purple in the rods.

With the development of several instruments, dysadaptation was found to result from many circumstances; and all the while the classifications of night blindness increased in number and kind. Commenting on the unsuccessful attempts to unify the concepts of night blindness, Birch-Hirschfeld (42) summed up the status in 1917: "The chief difficulty in explaining the nature of night blindness rests on the fact that we are dealing with a symptom rather than a uniform disease produced by a particular etiology." He presented a classification based on eleven causes, each with a different mechanism affecting visual purple. Thus it came to be believed that there were several kinds of night blindness. Acute epidemic or essential night blindness was regarded as due to dietary deficiency. During World War I, however, there were epidemics attributed to nondietary factors. Furthermore, it was pointed out that night blindness and dysadaptation were not synonymous, that disturbance in the transmissive mechanism, apart from the receptive tissue, could bring about night blindness by preventing effective operation of the visual purple.

In 1915 Wietfeld (43) suggested that essential or epidemic night blindness might be due to a lack of vitamins. Upon curing this form with carrot juice or liver, Zak (44) in 1917 stated that it was a manifestation of avitaminosis, although his studies did not permit him to

decide whether it was an independent disease or a symptom of scurvy. Hift (45) laid great emphasis on the concurrence of night blindness and scurvy. At the same time Birch-Hirschfeld (42) likewise specified vitamin deficiency as one of the primary influences in the pathogenesis of night blindness, citing scurvy, beriberi, and keratomalacia as examples without identifying the relation of night blindness. In 1923 Popovitch (46) suggested that it resulted from a deficiency in the fat-soluble vitamin since therapeutically active substances were rich in it. By testing the ability of rats to jump off a table in a dim light, after previous exposure to bright sunlight, Holm (47) demonstrated that vitamin A deficient rats had developed a well-defined night blindness. The administration of vitamin A to them resulted in a disappearance of symptoms. At the same time Fridericia and Holm (48) reported that vitamin A deficient rats placed in the dark after exposure to light showed a retarded regeneration of visual purple. Thus one form of night blindness, with dysadaptation due to impaired regeneration of visual purple, was linked with avitaminosis A.

Very largely on the basis of the latter studies (47, 48), night blindness came to be regarded also as the earliest sign of avitaminosis A. Of the delay in regeneration of visual purple, Fridericia and Holm said: "This symptom is an early one, being manifested as soon as the growth of the young rat stops and earlier than the onset of pronounced xerophthalmic symptoms." Even more emphatic was Holm: "The hemeralopia in the experimental-rats could be detected soon after the alimentation on food without fat-soluble A had begun, ... *at a stage where it was impossible to perceive any other sure signs of avitaminosis* except a slight failure to increase normally in weight."

This view that night blindness is the earliest sign of avitaminosis A gained ready acceptance in clinical medicine. In a text-book (49) on the clinical manifestations of avitaminoses, it is said: " ..... bilden sie eine besondere Trias, die allerdings beim gleichen Indivi-

duum nicht immer gleichzeitig, sondern meist in einer bestimmten zeitlichen Reihenfolge: Hemeralopie- Xerophthalmie-Keratomalacie, angetroffen wird." Several reasons probably contributed to this acceptance. Although originally the simultaneous presence of two or all three of the signs in the same person finally came to be noted, there was no common agreement at that time on the sequence of events. Subsequently knowledge concerning night blindness developed separately. Within the past 25 years there have been numerous recorded epidemics of night blindness. In that time there have been few or no reports on any high incidences of xerosis conjunctivae, although there have been recorded outbreaks of xerosis corneae and keratomalacia in which xerosis conjunctivae, alone, as the initial change, must certainly have been present earlier. Emphasis, however, was placed on the more severe stage, keratomalacia; indeed xerophthalmia more and more came to connote more strictly the corneal stage. As an advanced stage, its subsequence to night blindness was not questioned. Furthermore, night blindness was detected because of patient's complaint; but in xerosis conjunctivae, since visual acuity is not markedly affected, the patients are usually not concerned over the symptoms until inquiry directs attention to them.

When night blindness was said to be the earliest sign, it came to mean that it is a manifestation of mild avitaminosis A, either too short in duration or insufficiently severe in degree to produce xerophthalmia (50). This view gave fresh impetus to tests for dark adaptation as a means of detecting avitaminosis A, particularly the subclinical stage. With technical improvements it became possible to measure small deviations in dark adaptation. Since manifest night blindness was regarded as the earliest ocular sign of avitaminosis A, these small changes were understandably interpreted as a still earlier stage of the disturbance. All this has strengthened the notion that night blindness, or dysadaptation, is the earliest change.

Nevertheless, when the entire record of events is carefully con-

sulted, it is proper to raise three questions: Is night blindness a specific manifestation of avitaminosis A? Can night blindness result from vitamin A deficiency alone? Is night blindness the earliest sign of avitaminosis A? Each has a bearing on the usefulness of the adaptometer as a means of detecting subclinical avitaminosis A. The first two questions, however, may be considered jointly.

By almost every investigator of epidemic night blindness, from the very earliest to the more recent, its onset has been attributed to overexposure to bright light (4, 17, 33, 35-40, 42, 47, 48). Its occurrence predominantly among workers exposed to the sunlight for long hours, day after day, as in the fields and at sea, was at once suggestive and convincing. In accord with it were the observations that night-blind patients experienced no difficulty in seeing in early morning although it was much darker than in the evening (17, 48). Throughout the course of expanding and shifting views on the etiology of night blindness, investigators continued to lay stress on light; most of them designated it as the determining or precipitating influence. Deficient diet was regarded until recently only as a contributory factor. Other evidence added support to the view that light was a significant influence. For many years the standard treatment for night blindness was confinement in a dark room for 48 hours, or the use of dark glasses. The prompt efficacy of this treatment gave substance to the views about the influence of light in the causation of night blindness.

On the experimental side, it should be recalled that Fridericia and Holm succeeded in inducing night blindness and dysadaptation in vitamin A deficient rats only after exposing them to intense sunlight for several hours daily over a period of several weeks and then to artificial light for 20 minutes prior to the test (47, 48). Holm declared (47): "Hemeralopia does not develop through lack of fat-soluble-A-vitamin alone; *it is necessary also that the individuals be much exposed to light.*" It may well be that actinic rays have an aggravating effect on avitaminosis A; it should be borne in mind

that such a reaction has been noted in ariboflavinosis and pellagra. In any event, all these observations are pertinent to any consideration of the prevalent view that vitamin A deficiency alone produces night blindness as a specific manifestation. They also raise the question whether the present procedure in the tests for dysadaptation would permit detection of it in the subclinical stage.

The place of night blindness in the sequence of ocular manifestations is a matter fundamental to the early detection of avitaminosis A. When all circumstances are taken into account, it is quite possible that night blindness may not be the earliest ocular change. Reexamination of the very early records brings out the uncertainty in the matter and at the same time indicates the advisability of giving fuller consideration to xerosis conjunctivae. It is well to recall that one hundred years ago clinicians seeking signs for early detection of the syndrome debated this very question of whether night blindness or xerosis conjunctivae is earlier. There was marked divergence of opinion, but the evidence supported equally well, if not preponderantly, the priority of xerosis. For one thing, in Bitot's series of cases, the conjunctival spots occurred without night blindness. Besides, in some cases night blindness appeared only after the xerosis was far advanced. Bitot regarded xerosis as the herald of night blindness.

Although the recorded epidemics of night blindness in which xerosis was not mentioned have doubtless favored acceptance of night blindness as the earliest manifestation of avitaminosis A, the view really hinges on the animal experiments of Fridericia and Holm (47, 48). It should be noted that when they stated (48) that dysadaptation preceded pronounced xerophthalmic symptoms, they meant that dysadaptation preceded corneal involvement, which is an advanced or late stage. Furthermore, when Holm (47) stated that night blindness developed in the rats before any perceptible signs of avitaminosis except retardation in growth, he was judging by three signs not recorded for man: enophthalmus, loss

of ciliary hair, and a peculiar lacrimal secretion. He did not mention looking for xerotic changes in the conjunctivae other than to state that because of physical conditions it is impossible to produce Bitot's spots in rats. Certainly on the basis of neither study can it be said that night blindness precedes xerosis conjunctivae. In fact, the observations, both clinical and experimental, would seem to cast some doubt on the validity of the prevalent view that night blindness is the first ocular sign of avitaminosis A.

Present-day work does not dispel this doubt. In studies on adaptation with sensitive equipment, often the validity of the data on avitaminosis A has not been supported by therapeutic evidence. In other instances it has been shown that small differences supposedly representing improvement from vitamin A therapy were probably learning responses or instrumental artefacts (51, 52, 53).

This background would seem to warrant reopening the question whether xerosis or night blindness is the earlier manifestation. While the old observations serve to revive the issue, they cannot settle it. Then both conditions were diagnosed only in their advanced stages and in a way—xerosis by gross examination and night blindness by history—which is inconclusive on the point of priority. For this it is necessary to have observations with sensitive instruments on early dysadaptation and xerosis, noting their concurrence or order of appearance. With the calibrated adaptometer and the biomicroscope, this became possible. In the present study dysadaptation did not precede the xerosis conjunctivae. Indeed, dysadaptation was not specifically correlated with the degree of conjunctival change.

It is generally accepted that characteristic lesions in the eye are not the only changes in avitaminosis A, nor are they regarded as the first. However, the intimation that skin lesions, under such varied names as follicular hyperkeratosis, phrynoderma, and xeroderma, represent the initial manifestation (54), finds no support from histopathological studies on experimental animals. In the

"spot" cases of the present study, only occasionally were possible dermal lesions noted; then they were so indefinite as to be questionable. None were seen in persons with less severe eye lesions. In the entire series, therefore, gross cutaneous did not precede ocular changes.

In suggesting biomicroscopic examination of the eye as a means of detecting early avitaminosis A, it is not meant to imply that the ocular lesion is the sole, the first, or the most important change. Xerophthalmia is not synonymous with avitaminosis A. Histopathological examinations on both humans and animals have shown that avitaminosis A is characterized by widespread epithelial changes throughout the body, for example, the respiratory, paraocular, and renal, as well as the ocular organs (55, 56, 57). Wolbach and Howe (56) have stated that xerophthalmia is not the earliest manifestation of avitaminosis A in the rat. For human beings there is very little evidence on what is the initial site and the sequence of sites undergoing change.

Nevertheless, among the organs showing early change, the eyes are a favorable site for detecting vitamin A involvement, for they are accessible to observation or test. There is another point of advantage: the initial lesion in the eye occurs in the conjunctiva. Inspection for gross changes, including Bitot's spots, may be used in screening advanced cases, which may be subgrouped, if desired, according to the number of zones affected. Biomicroscopic examination detects subgross changes of all gradations which may be classified according to severity and extent. Hence, by combined gross and microscopic examinations, it is possible to determine all stages of xerosis and thus to grade the avitaminosis A.

Especially does the biomicroscopic examination of the bulbar surface present several additional advantages: (1) it shows the early changes in the conjunctiva—site of the initial ocular lesion in avitaminosis A—that are not visible grossly; (2) it is a rapid, convenient, and objective method for detecting the very early avita-

minosis A; (3) it permits a simultaneous examination of the limbus and cornea for early ariboflavinosis, from which avitaminosis A is easily differentiated; (4) it provides a much-needed means for ascertaining the dietary requirements for both vitamin A and riboflavin.

In the present study, the examination of conjunctivae both grossly and biomicroscopically shows a high prevalence of avitaminosis A in this low-income group. It is so high as to seem at first glance almost incredible, but it is substantiated on several grounds.

In reporting on a national dietary survey Stiebeling and Phipard stated (58): "Taking 6,000 International Units per day as the allowance for the adult man, . . . it is estimated that the lowest 25 per cent of the diets [for all of the white families represented by the study] furnished 2,000 or less International Units a requirement unit a day, and the lowest 75 per cent, less than 4,500 International Units a day." In the cities of the North Atlantic region, including New York City, they found that in the group with a weekly per-capita expenditure for food between $1.25 and $1.87, 67 per cent had less than 2,000 International Units, 20 per cent had between 2,000 and 3,999 Units, and 9 per cent between 4,000 and 5,999 Units. At least 90 per cent were thus receiving less than the estimated required amount of vitamin A. In the present study, the prevalence of avitaminosis A in the comparably low-income group was more than 90 per cent.[2] These figures strikingly bear out the dietary data while the latter, in turn, account for the high prevalence, suggesting that dietary deficiency was largely responsible.

In addition, it is not at all unlikely that in some instances other factors contributed to the prevalence. For example, it is conceivable that certain acute illnesses disturbing the vitamin A economy may have brought on the avitaminosis or accentuated existing lesions so

[2] A lower prevalence would be expected in higher income groups. Upon examination of 25 adults in a medium income group, 16 showed definite conjunctival changes. Five persons in the group had gross spots. It is more than likely that avitaminosis A is one of the more commonly occurring deficiency diseases and is present in a considerable proportion of the population.

that in convalescence even an abundant amount of the essential in the diet would not be sufficient for rapid restoration. With a slightly inferior diet recovery would not be complete for an indefinite period.

Furthermore, with manifest conjunctival lesions in 45 per cent of the persons, a sizeable number with less pronounced changes visible only with the biomicroscope would be expected. But above all, the response of the affected persons to the specific therapy attests to the actuality of avitaminosis A in so large a proportion of the group.

Upon administration of therapy, recession is similar in type to that in ariboflavinosis: obliteration of vessels and dissipation of opacities. The striking feature, however, is the very long period required for complete recovery, a matter of months even with therapy of high potency. This is reasonable considering that when the eyes show such profound change, many epithelial structures throughout the body are known to be simultaneously affected. Restoration of all this epithelium takes time.

These results indicate that complete recovery from this deficiency disease is not so rapid as it is popularly reported. This protracted recovery, even with high dosage of vitamin A, also casts a significant light on therapeutic practice in avitaminoses. Currently it is often asserted that adequate diet corrects deficiency diseases. In a sense this is true if time is no consideration. But if therapy of high potency brings about complete recovery only after an extended period, an optimum diet might be expected to require a very much longer time. It seems necessary to take the view that persons affected with deficiency diseases need intensive specific therapy for most rapid recovery. Obviously, an optimum diet should be instituted for its supplementary nutritive value, its protection against outbreak of other deficiencies, and for establishment of satisfactory dietary practice by the patient. Then when therapy is withdrawn upon recovery, the satisfactory dietary habits suffice for maintenance.

The use here of 100,000 I.U. of vitamin A daily is not to be construed as a recommendation or precedent that this amount is necessary for maximum rapid therapeutic results. In the present study it was essential to administer an amount that would ensure maximum response. It is certain that tissues have critical rates of response and that doses in excess of the amounts satisfying those rates have no further effect. It is common experience that effective therapeutic dosage for an avitaminosis is at least five to six times the maintenance requirement. Actually, therefore, it may be that daily levels of vitamin A between 25,000 and 50,000 I.U., for example, will be found sufficient to produce maximum therapeutic response. That is to be determined.

Summary

Of 143 persons in a low-income group, 45 per cent had gross and another 54 per cent had microscopic ocular lesions characteristic of avitaminosis A. The ocular condition was xerosis conjunctivae.

Following administration of vitamin A as specific therapy to a part of the group, the conjunctival lesions in nine persons have now completely disappeared, as judged in all instances by biomicroscopic examination. In all others receiving therapy, the conjunctival lesions have markedly receded to the point of near disappearance.

In all cases the striking feature is the very long period of time required for complete recovery, a matter of months even with therapy of high potency.

Those persons not receiving therapy have shown no improvement.

It is suggested that xerosis probably precedes night blindness as an early sign of avitaminosis A.

For detection of early avitaminosis A in surveys, the biomicroscopic examination is recommended as a simple, convenient, objective method. When it is combined with gross examination, all degrees of xerosis may be graded according to severity and extent.

The marked prevalence of avitaminosis A in this low-income group, objectifying and validating previous dietary data, suggests its relatively frequent occurrence in the population at large.

References

1. Kruse, H. D.; Palmer, C. E.; Schmidt, W.; and Wiehl, Dorothy G.: Medical Evaluation of Nutritional Status. I. Methods Used in a Survey of High School Students. The Milbank Memorial Fund *Quarterly*, July, 1940, xviii, No. 3, pp. 257-283.

2. Kruse, H. D.; Sydenstricker, V. P.; Sebrell, W. H.; and Cleckley, H. M.: Ocular Manifestations of Ariboflavinosis. *Public Health Reports*, January 26, 1940, 55, pp. 157-169.

3. Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M.; and Kruse, H. D.: The Ocular Manifestations of Ariboflavinosis. A Progress Note. *The Journal of the American Medical Association*, June 22, 1940, 114, pp. 2437-2445.

4. Bitot: Mémoire sur une lésion conjonctivale non encore décrite, coïncidant avec l'héméralopie. *Gazette Hebdomadaire de Médecine et de Chirurgie*, May 1, 1863, 10, No. 18, pp. 284-288. Also *Gazette Médicale de Paris*, July 4, 1863, 18, No. 27, pp. 435-438.

5. Cohn, H.: Ueber Xerosis Conjunctivae. Breslau. Habilitations-schrift. 1868, 43 pp.

6. Schmidt, Joh. Adam: Ueber die Krankheiten des Thränenorgans. Wien, Joseph Geistinger. 1803, 350 pp.

7. Benedict, T. W. G.: Handbuch der praktischen Augenheilkunde. III: Von den chronischen Krankheiten der Augenlieder, der Bindehaut, Kornea, Sklerotika und Regenbogenhaut. Leipzig, Dyk'schen Buchhandlung. 1824, 159 pp.

8. Mackenzie, William: A Practical Treatise on the Diseases of the Eye. From the last London edition, Boston, Carter, Hendee and Company, 1833, 703 pp.

9. Lawrence, W.: A Treatise on the Diseases of the Eye. London, John Churchill, 1833, 364 pp.

10. Travers, Benjamin: A Synopsis of the Diseases of the Eye, and their Treatment: To Which are Prefixed a Short Anatomical Description and a Sketch of the Physiology of that Organ. 2nd edition, London, Longman, Hurst, Rees, Orme and Brown. 1821, 462 pp.

11. Jäger: Uebersicht der in der chirurgischaugenärztlichen Klinik des königl. Universitätskrankenhauses zu Erlangen vom 1. October 1828 bis zum I. October 1829 behandelten Krankheitsfälle und verrichteten Operationen. *Medicinisch-chirurgische Zeitung*, 1830, 1, pp. 28-32.

12. Klingsohr, E.: Die Ueberhautung der Bindehaut. Inaugural-Abhandlung, Erlangen, Kunstmann'schen Schriften. 1830, 36 pp.

13. v. Ammon: Beobachtungen, Ansichten und Zweifel über die Entstehung der Xerosis conjunctivae. *Zeitschrift für die Ophthalmologie*, 1831, 1, pp. 65-79.

14. Gama Lobo: *Gazeta Medica de Lisboa*, August 28, 1865, No. 16, p. 430; September 13, 1865, No. 17, p. 466. Cited by Ullersperger, B.: Brasilianische Augenentzündung. *Klinische Monatsblätter für Augenheilkunde*, 1866, 4, pp. 65-75.

15. Blessig: Ueber Xerose des Bindehautepithels und deren Beziehung zur Hemeralopie. *St. Petersburger Medicinische Zeitschrift*, 1866, 11, pp. 343-354.

16. Förster: Beziehungen der Allgemein-Leiden und Organ-Erkrankungen zu Veränderungen und Krankheiten des Sehorgans. Handbuch der gesammten Augenheilkunde, redigirt von A. Graefe und T. Saemisch, 7; *Pathologie und Therapie* (Theil 5, Capitel XIII), pp. 59-234. Leipzig, Verlag von Wilhelm Engelmann, 1877.

17. de Gouvêa, H.: Beiträge zur Kenntniss der Hemeralopie und Xerophthalmie aus Ernährungsstörungen. *Graefe's Archiv für Ophthalmologie*, 1883, 29 (Abtheilung I), pp. 167-200.

18. Thalberg, J.: Zur Casuistik der durch Inanitionszustände bedingten Hornhautgangrän. *Archiv für Augenheilkunde*, 1883, 12, pp. 315-332.

19. Schoeler: Beitrag zu den xerotischen Hornhautleiden unter Aufführung einer neuen, bisher von mir nicht beobachteten Form dieses Leidens nach Entziehungsdiät. *Berliner Klinische Wochenschrift*, 1887, 24, pp. 979-982.

20. Blegvad, O.: Xerophthalmia, Keratomalacia and Xerosis Conjunctivae. *American Journal of Ophthalmology*, February, 1924, 7 (Series 3), No. 2, pp. 89-117.

21. Mori, M.: Ueber den sog. Hikan (Xerosis conjunctivae infantum ev. Keratomalacie). *Jahrbuch für Kinderheilkunde und Physische Erziehung*, 1904, 59, (9. Band der dritten Folge): pp. 175-195.

22. Falta, W. and Noeggerath, C. T.: Fütterungsversuche mit künstlicher Nahrung. *Beiträge zur Chemischen Physiologie und Pathologie*, 1906, 7, pp. 313-322.

23. Knapp, P.: Experimenteller Beitrag zur Ernährung von Ratten mit künstlicher Nahrung und zum Zusammenhang von Ernährungsstörungen mit Erkrankungen der Conjunctiva. *Zeitschrift für Experimentelle Pathologie und Therapie*, 1909, 5, pp. 147-169.

24. McCollum, E. V. and Davis, M.: The Necessity of Certain Lipins in the Diet During Growth. *The Journal of Biological Chemistry*, 1913, 15, pp. 167-175.

25. Osborne, T. B. and Mendel, L. B.: The Influence of Butter-fat on Growth. *The Journal of Biological Chemistry*, 1913-14, 16, pp. 423-437.

26. Osborne, T. B. and Mendel, L. B.: The Influence of Cod-liver Oil and Some Other Fats on Growth. *The Journal of Biological Chemistry*, 1914, 17, pp. 401-408.

27. Goldschmidt, M.: Experimenteller Beitrag zur Aetiologie der Keratomalacie. *Archiv für Ophthalmologie*, 1915, 90, pp. 354-403.

28. Freise, E.; Goldschmidt, M.; and Frank, A.: Experimentelle Beiträge zur Aetiologie der Keratomalazie. *Monatsschrift für Kinderheilkunde*, 1916, 13, pp. 424-430.

29. Bloch, C. E.: Lidelser hos Smaaborn opstaaet paa Grund af Fedtmangel. Xerophthalmia et Dystrophia alipogenetica. *Ugeskrift for Laeger*, March 1, 1917, 79, pp. 309-325; March 8, 1917, 79, pp. 349-370.

30. McCollum, E. V. and Simmonds, N.: A Biological Analysis of Pellagra-Producing Diets. II. The Minimum Requirements of the Two Unidentified Dietary Factors for Maintenance as Contrasted with Growth. *The Journal of Biological Chemistry*, 1917, 32, pp. 181-193.

31. Lee, T'ao: Historical Notes on Some Vitamin Deficiency Diseases in China. *The Chinese Medical Journal*, September, 1940, 58, No. 3, pp. 314-323.

32. Ishihara, S.: Zur Aetiologie der idiopathischen Hemeralopie bzw. Xerosis conjunctivae. *Klinische Monatsblätter für Augenheilkunde*, 1913, 51, (Neu Folge *15*), pp. 596-603.

33. Graefe, Alfred: Beiträge zum Wesen der Hemeralopie. *Archiv für Ophthalmologie*, 1859, 5, (Abth. I), pp. 112-127.

34. Cless, G.: Die Gesundheitsverhältnisse der höheren Civilstrafanstalten des Königreichs Württemberg. *Deutsche Vierteljahrsschrift für öffentliche Gesundheitspflege,* 1879, 11, pp. 393-407.

35. Dumas, A.-J.-A.: Contribution a l'étude de l'héméralopie essentielle et de son traitement. Thèse pour le doctorat en médecine. Paris, 41 pp. (1889).

36. Kubli, T.: Zur Lehre von der epidemischen Hemeralopie. *Archiv für Augenheilkunde,* 1887, 17, pp. 409-411.

37. Krienes, Hans: Ueber Hemeralopie, speziell akute idiopathische Hemeralopie. Wiesbaden, J. F. Bergmann, 1896, 185 pp.

38. Toporoff, A.: Po voprosu ob etiologii povalnoi kurinoi sliepoti v voiskakh. (On the Question of Epidemic Night Blindness in the Army.) *Voyenno-Meditsinskiy Jurnal,* 1886, 156, (Part 2, Section 3), pp. 27-42.

39. Groenouw, A.: Beziehungen der Allgemeinleiden und Organerkrankungen zu Veränderungen und Krankheiten des Sehorganes: Erkrankungen der Atmungs-, Kreislauf-, Verdauungs-, Harn-, und Geschlechtsorgane, der Haut und der Bewegungsorgane, Konstitutionsanomalien, erblichs Augenkrankheiten und Infektionskrankheiten. *Graefe-Saemisch Handbuch der gesamten Augenheilkunde* (herausgegeben von T. Saemisch), 11, Abteilung 1, Teil I, Seite 1-823. Zweite neubearbeitete Auflage. Leipzig, Wilhelm Engelmann, 1904.

40. Parinaud: L'héméralopie et les fonctions du pourpre visuel. *Comptes Rendus Hebdomadaires des Séances de L'Académie des Sciences,* 93, pp. 286-287. Also *Gazette Médicale de Paris,* 1881, 52, (6. série, tome III), p. 484.

41. Treitel, Th.: Ueber Hemeralopie und Untersuchung des Lichtsinnes. *Graefe's Archiv für Ophthalmologie,* 1885, 31, (Abth. I), pp. 139-176.

42. Birch-Hirschfeld, A.: Ueber Nachtblindheit im Kriege. *Archiv für Ophthalmologie,* 1917, 92, pp. 273-340.

43. Wietfeldt: Avitaminose als Ursache der Nachtblindheit im Felde. *Münchener Medizinische Wochenschrift* (Feldärztliche Beilage), December 14, 1915, 62, (II. Hälfte), p. 1743.

44. Zak, E.: Beobachtungen an Hemeralopie- und Skorbutkranken. *Wiener Klinische Wochenschrift,* 1917, 30, pp. 592-595.

45. Hift, R.: Beobachtungen über Skorbut und Hemeralopie. *Wiener Klinische Wochenschrift,* 1918, 31, pp. 939-942.

46. Popovitch, A.: L'héméralopie de cause alimentaire. *Archives D'Ophtalmologie,* 1923, 40, p. 315.

47. Holm, E.: Demonstration of Hemeralopia in Rats Nourished on Food Devoid of Fat-Soluble-A-Vitamin. *The American Journal of Physiology,* 1925, 73, pp. 79-84.

48. Fridericia, L. S. and Holm, E.: Experimental Contribution to the Study of the Relation between Night Blindness and Malnutrition. Influence of Deficiency of Fat-Soluble A-Vitamin in the Diet on the Visual Purple in the Eyes of Rats. *The American Journal of Physiology,* 1925, 73, pp. 63-78.

49. György, P.: Xerophthalmie und Keratomalacie. Kapitel in: Avitaminosen und verwandte Krankheitszustände. Herausgegeben von W. Stepp und P. György. Berlin, Julius Springer. 1927, 817 pp. (172).

50. Medical Research Council: Vitamins: A Survey of Present Knowledge. Special Report Series, No. 167. London, His Majesty's Stationery Office, 1932, 332 pp.

51. Palmer, C. E. and Blumberg, H.: The Use of a Dark Adaptation Technique (Biophotometer) in the Measurement of Vitamin-A Deficiency in Children. *Public Health Reports*, 1937, 52, pp. 1403-1419.

52. Palmer, C. E.: The Dark Adaptation Test for Vitamin-A Deficiency. *American Journal of Public Health*, 1938, 28, pp. 309-315.

53. Hunt, E. P. and Palmer, C. E.: Medical Evaluation of Nutritional Status. II. Measurement of Visual Dark Adaptation with the Adaptometer. The Milbank Memorial Fund *Quarterly*, October, 1940, 18, No. 4, pp. 403-424.

54. Lehman, E. and Rapaport, H. G.: Cutaneous Manifestations of Vitamin A Deficiency in Children. *The Journal of the American Medical Association*, February 3, 1940, 114, No. 5, pp. 386-393.

55. Leber, Th.: Ueber die Xerosis der Bindehaut und die infantile Hornhautverschwärung nebst Bemerkungen über die Entstehung des Xerophthalmus. *Graefe's Archiv für Ophthalmologie*, 1883, 29, (Abtheilung III), pp. 225-290.

56. Wolbach, S. B. and Howe, P. R.: Tissue Changes Following Deprivation of Fat-Soluble A Vitamin. *The Journal of Experimental Medicine*, 1925, 42, pp. 753-777.

57. Van Leersum, E. C.: Vitamin A Deficiency and Urolithiasis. *British Medical Journal*, November 12, 1927, ii, pp. 873-874.

58. Stiebeling, H. K. and Phipard, E. F.: Diets of Families of Employed Wage Earners and Clerical Workers in Cities. United States Department of Agriculture, Circular No. 507, Washington, D. C., U. S. Government Printing Office, 1939, 140 pp.

Explanation of Figures

Fig. 1. 1st Row, Person A; 2nd Row, Person B. On each row from left to right, the zones are presented in the following order: right temporal, right nasal, left nasal, and left temporal. In each instance the eye has been rotated to expose more completely the particular zone under discussion.

3rd Row, the first two illustrations are the right and left eye, respectively, of Person B. The third and fourth illustrations are the right and left nasal zone, respectively, of Person C, with the eyes rotated temporally. Persons A and B have a spot in each zone, i.e., the nasal and temporal zones of both eyes; C only in each of the nasal zones. They also form a descending series in severity.

Fig. 2. 1st Row, Person D; 2nd Row, Person E; 3rd Row, Person F. On each row from left to right, the first two pictures show the right and left eye, respectively. The third and fourth illustra-

tions are of the right and left nasal zone, respectively, with the eyes rotated temporally.

Spots may be seen in all of the nasal zones of each eye in this series: the rows form a descending series in severity.

The entire series, including both Figures 1 and 2, shows a diminution in the pigmentation of the lesions from Person A to Person F.

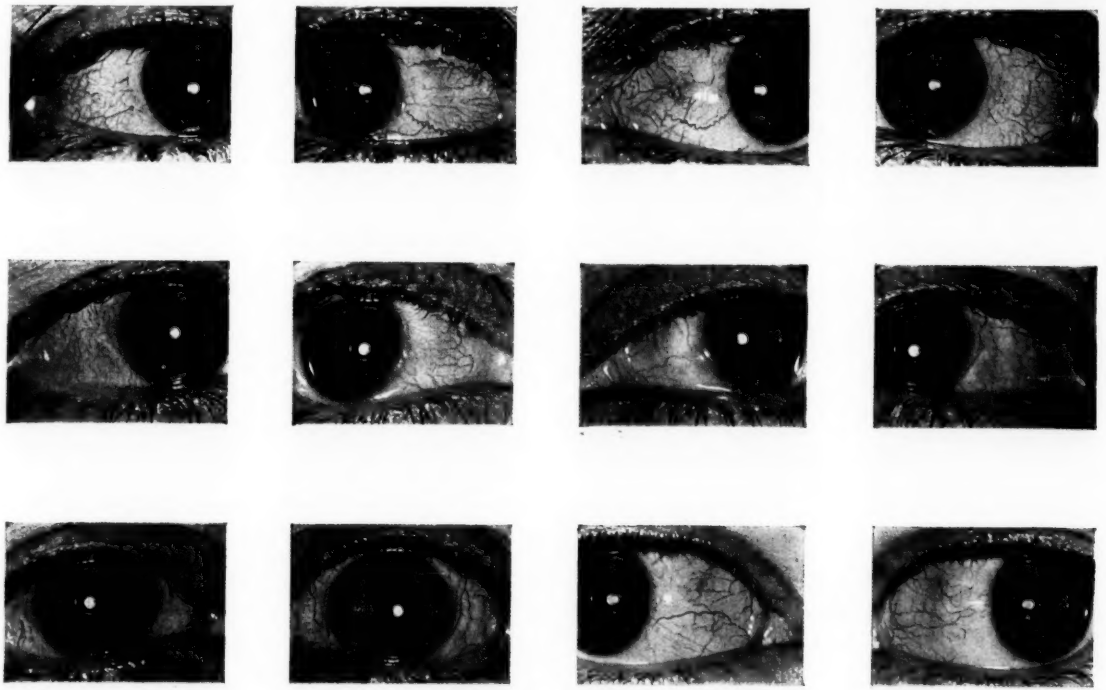

Fig. 1. See explanation on page 239.

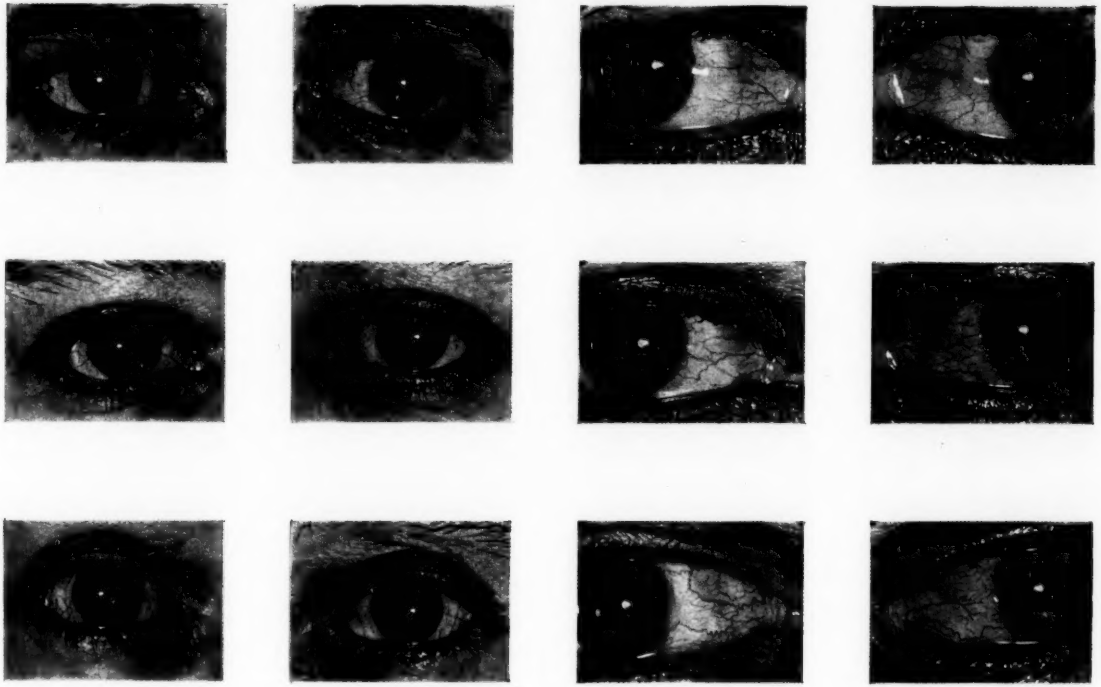

Fig. 2. See explanation on pages 239 and 240.

MEDICAL EVALUATION OF NUTRITIONAL STATUS[1]

V. PREVALENCE OF DEFICIENCY DISEASES IN THEIR SUBCLINICAL STAGE

DOROTHY G. WIEHL AND H. D. KRUSE, M.D.

WITH the development of methods for diagnosing nutritional deficiencies while the condition is in a very early or mild stage, it becomes possible to determine the prevalence of such deficiency diseases in various groups of the population. The frank or fully developed deficiency diseases, such as pellagra, scurvy, and beriberi, which can be diagnosed by usual clinical methods, occur to some extent in the United States, but data from extensive and careful analyses of American diets have provided important, though inferential, evidence that a very large number of persons are malnourished with respect to one or more essential food elements. Research in recent years has disclosed the bodily changes which result from insufficient amounts of some of the specific nutrients when deprivation has not been severe enough to produce frank deficiency diseases. For a few of the subclinical changes caused by specific deficiencies, diagnostic procedures are now available which can be used for surveys of large groups of persons to determine the prevalence of mild cases of deficiency diseases.

From an investigation in New York City on Medical Evaluation of Nutritional Status, which is a cooperative study conducted by the Cornell University Medical College, the Milbank Memorial Fund, the New York City Department of Health, and the United States Public Health Service, with assistance from the WPA, some data on prevalence of four nutritional deficiencies are presented in this report. In this Study, which has been described (1), emphasis has

[1] This paper is the fifth of a series from a cooperative investigation by the Cornell University Medical College, Department of Public Health and Preventive Medicine and Department of Pediatrics; the Milbank Memorial Fund; the New York City Department of Health; and the United States Public Health Service, Division of Public Health Methods.

The cooperating agencies have been assisted in carrying out this investigation by the Work Projects Administration for the City of New York, Official Project No. 65-1-97-21, W. P. 24, "Medical Evaluation of Nutritional Status."

been placed on the appraisal of procedures, and in the two years during which examinations have been made, new tests have been added to the procedures as they became available. For the present report results of examinations for avitaminosis A, ariboflavinosis, anemia, and low ascorbic acid levels in blood plasma are tabulated for those persons in the Study who received all or nearly all of the tests for these deficiencies.

Diagnostic Procedures

Avitaminosis A reported here is based on changes in the conjunctiva detected by an examination with a biomicroscope under slit-lamp illumination. The examination and criteria for pathological changes have been fully described in another report (2) from this Study. Cases are classified in three stages according to the degree of light transmission: (1) those with minimum change, showing definite translucency; (2) those with somewhat more advanced change, characterized by opacity; and (3) cases in which opaque areas are thickened to the point of elevation, termed spot cases. Conjunctival alteration may be present in either the nasal or temporal zone, or both, of either or both eyes, and the case is classified according to the most advanced stage noted in one or more zones.

Ariboflavinosis cases are diagnosed on the basis of keratitis disclosed by a biomicroscopic examination with slit-lamp illumination (3, 4). Persons showing only vascular arcades around the limbus have not been counted as deficient, but those with capillaries noted as having extended into the cornea in one or both eyes have been counted as cases of ariboflavinosis. The cases are subdivided into three groups as follows: (1) those with short "twigs" in cornea of either eye or each eye; (2) those with 1 to 4 capillary "streamers" in cornea of either eye or each eye; and (3) those with 5 or more "streamers" in either eye or each eye.

The determination of the amount of hemoglobin in the blood to select persons with anemia was based upon the colorimetric deter-

mination of oxyhemoglobin by the Evelyn method, using the photoelectric colorimeter (5).

Ascorbic acid level of fasting plasma was determined on a macro sample by the photoelectric colorimeter method (6), based upon the reduction of 2:6 dichlorophenol-indophenol. The evidence on vitamin C nutrition derived from plasma ascorbic acid differs in its significance from the evidence on vitamin A, riboflavin, and iron. For the latter three, the examination reveals changes which have been produced over a period of time by subnormal nutrition, whereas plasma vitamin C may vary within a short time, or from day to day, and does not necessarily reflect the nutritive state of the body with respect to vitamin C.

Persons Examined

Examinations on high school students from families of low income and of relatively high income furnished the major part of the data in this report.

The low-income group is from Seward Park High School, in the lower East Side district of Manhattan. Examinations were made in the winter of 1940-1941 on about 500 pupils, most of whom were examined for all four deficiencies mentioned above. The economic status of the families of these pupils is revealed in Table 1, which

Table 1. Weekly income reported by families with children who were examined in Seward Park High School in the winter of 1940-1941.

Income Status	Per Cent of Total	Number of Families With Income Known
All Families	100.0	473
Relief		
WPA	8.9	42
All Other	12.3	58
Non-Relief		
Less Than $20.00	10.1	48
$20.00—$34.99	40.2	190
$35.00 and Over	28.5	135

gives the weekly income reported to a home visitor, who usually interviewed the child's mother. Twenty-one per cent of the families were receiving assistance; either a member of the family had work relief, or the family was receiving some type of aid from a private or public relief agency. Nearly 30 per cent of the families had an income from earnings of $35 or more per week, leaving about 50 per cent with less than $35 per week and not on relief. The families are predominantly Jewish, and parents of the examined students were largely foreign born. Most of the non-Jewish children were of Italian parentage, one or both parents being foreign born.

The high-income group includes about 350 pupils in a private school in New York City, the Fieldston School of the Ethical Culture Schools. Children in this group were examined in the early spring of 1940 and did not have an examination of the conjunctiva for avitaminosis A. For nearly all pupils in this group, data are available on hemoglobin values, plasma ascorbic acid, and keratitis.

During the period from July, 1939 to May, 1941, hemoglobin values and plasma ascorbic acid levels have been determined for 136 persons employed by the WPA, and for a few more, one of the determinations was made. In addition, 138 such employes received an eye examination to detect the presence of keratitis, and 143 received an examination to discover conjunctival changes characteristic of avitaminosis A. In relatively few instances did the same person receive all four of these tests.

Prevalence of Three Deficiencies in a High-Income Group

Among the pupils in the high-income group, few persons showed evidence of a dietary deficiency of ascorbic acid, iron, or riboflavin. Prevalence rates for deficiencies in each of these nutrients are given in Table 2. None of the boys was found to have hemoglobin values significantly low[3] and none showed vascularization of the cornea

[3] No accepted and generally approved standards for satisfactory hemoglobin values for boys and girls between 12 and 20 years of age are available. Tentative standards used here

(Continued on page 245)

Classification of Findings	Percentage of Total			Number Examined		
	Both Sexes	Boys	Girls	Both Sexes	Boys	Girls
	ASCORBIC ACID IN PLASMA					
Total	100.0	100.0	100.0	342	178	164
0.00–0.39 mg. %	2.9	3.9	1.8	10	7	3
0.40–0.59 mg. %	2.6	2.8	2.4	9	5	4
0.60–0.99 mg. %	21.3	24.7	17.7	73	44	29
1.00 or More mg. %	73.1	68.5	78.0	250	122	128
	HEMOGLOBIN CLASSIFICATION					
Total	100.0	100.0	100.0	336	175	161
Below "Standard"[1]	1.5	0	3.1	5	0	5
Standard or Higher	98.5	100.0	96.9	331	175	156
	KERATITIS—ARIBOFLAVINOSIS					
Total	100.0	100.0	100.0	354	183	171
Vessels in Cornea	2.3	0	4.7	8	0	8
No Corneal Invasion	97.7	100.0	95.3	346	183	163

[1] For standards for hemoglobin used, *see* footnote 2.

Table 2. Prevalence of three nutritional deficiencies among high school students from high-income families in New York City.

under slit-lamp examination. Plasma ascorbic acid levels less than 0.6 mg. per cent were found for 6.7 per cent of boys. Among girls, some cases of each deficiency were diagnosed. Hemoglobin values less than 12.0 grams per 100 cc. of blood were found for 5 girls, or 3.1 per cent; all had mild anemia with hemoglobin values between 10.0 and 12.0 grams. Examination of the cornea showed eight girls, or 4.7 per cent, had vascularization characteristic of a mild riboflavin deficiency; and plasma ascorbic acid levels were less than 0.6 mg. per cent for 4.2 per cent of the group.

were derived from a special analysis of this high-income group and take account of both chronological and physiological age. The values used for a minimum level were: for boys, under 13 years of age, 12.0 gms. per 100 cc.; 13 years and older, with no pubic hair, 12.0 gms.; with sparse pubic hair, 12.8 gms.; with moderate or abundant pubic hair, 13.5 gms.; for all girls, 12.0 gms. Changes in hemoglobin levels by age during adolescence have been described (7) and, in a later report, a detailed analysis of the relation of physiological development to changes in hemoglobin levels will be presented.

All of the girls showing one of these deficiencies had all three tests, and in no case was there a multiple deficiency. Thus, among 161 girls with all three tests, there were twenty, or 12.4 per cent, with one deficiency. Results of all three tests are available for 336 boys and girls, and 9.5 per cent showed evidence of a nutritional deficiency in either iron, ascorbic acid, or riboflavin.

Prevalence of Four Deficiencies in a Low-Income Group

The prevalence of four nutritional deficiencies among the pupils from low-income families is shown in Table 3, and the rates are strikingly different from those for the high-income group with the exception of that for low hemoglobin values. The percentage of children showing some stage of avitaminosis A was 86.6; the percentage with mild ariboflavinosis was 75.8; the percentage with plasma ascorbic acid less than 0.60 mg. per cent was 49.9; and the percentage with hemoglobin values below the assigned minimum was 3.3. Boys more frequently than girls were found to show relatively advanced stages of these deficiencies except iron. Thus, among boys examined for avitaminosis A, 9.4 per cent was in the "spot case" class and among girls, there was 5.6 per cent; keratitis with 5 or more capillary "streamers" in the cornea was found in 10.8 per cent of boys and 4.2 per cent of girls; and the comparative percentages for boys and girls with plasma ascorbic acid below 0.60 mg. per cent were 55.6 and 42.3, respectively. Anemia, on the other hand, was more prevalent among girls; but, for both sexes, the few cases considered subnormal were only slightly below the minimum hemoglobin levels.

When comparisons are made between rates for the total prevalence of each deficiency disease, the proportions in each according to severity should be borne in mind. The cases of avitaminosis A and ariboflavinosis each have been arbitrarily classified into three stages; but the gradations of severity of one deficiency are not equivalent to those of the other. For example, stage 3 of avitaminosis A repre-

Classification of Findings	Percentage of Total			Number Examined		
	Both Sexes	Boys	Girls	Both Sexes	Boys	Girls
	CONJUNCTIVAL CHANGE—AVITAMINOSIS A					
Total	100.0	100.0	100.0	494	278	216
Spot Case	7.7	9.4	5.6	38	26	12
Opacity	41.3	40.6	42.1	204	113	91
Marked Translucency						
3–4 Zones	33.4	34.5	31.9	165	96	69
1–2 Zones	4.3	3.6	5.1	21	10	11
No Marked Translucency	13.4	11.9	15.3	66	33	33
	KERATITIS—ARIBOFLAVINOSIS					
Total	100.0	100.0	100.0	495	279	216
5 or More Streamers	7.9	10.8	4.2	39	30	9
1–4 Streamers	34.7	32.3	38.0	172	90	82
Twigs Only	33.1	32.6	33.8	164	91	73
No Corneal Invasion	24.2	24.4	24.1	120	68	52
	ASCORBIC ACID IN PLASMA					
Total	100.0	100.0	100.0	425	241	184
0.00–0.39 mg. %	32.0	34.0	29.3	136	82	54
0.40–0.59 mg. %	17.9	21.6	13.0	76	52	24
0.60–0.99 mg. %	25.2	24.1	26.6	107	58	49
1.00 or More mg. %	24.9	20.3	31.0	106	49	57
	HEMOGLOBIN CLASSIFICATION					
Total	100.0	100.0	100.0	425	241	184
Below "Standard"[1]	3.3	2.5	4.3	14	6	8
Standard or Higher	96.7	97.5	95.7	411	235	176

[1] For standards for hemoglobin, *see* footnote 2.

Table 3. Prevalence of four nutritional deficiencies among high school students from low-income families.

sents a more advanced stage of xerosis than stage 3 of ariboflavinosis does of keratitis.

With such high proportions of these high school students deficient in vitamin A, riboflavin, and ascorbic acid, it is obvious that many had multiple deficiencies. In fact, if only vitamin A and ribo-

Deficiencies[1]	Boys		Girls	
	No.	Per Cent	No.	Per Cent
Total	241	100.0	184	100.0
4: A+R+C+ Iron	1	0.4	4	2.2
3: A+R+C	83	34.4	42	22.8
A+R+ Iron	2	0.8	0	0
A+C+ Iron	2	0.8	0	0
R+C+ Iron	0	0	1	0.5
2: A+R	77	32.0	66	35.9
A+C	27	11.2	16	8.7
A+ Iron	0	0	1	0.5
R+C	13	5.4	11	6.0
R+ Iron	0	0	1	0.5
C+ Iron	1	0.4	1	0.5
1: A	17	7.1	24	13.0
R	7	2.9	14	7.6
C	7	2.9	3	1.6
None	4	1.7	0	0

[1] A is vitamin A, R is riboflavin, C is vitamin C (ascorbic acid.)

Table 4. Percentage of students in low-income group who had specified combinations of deficiency diseases.

flavin are considered, two-thirds (66.2 per cent) of the 494 children receiving both examinations showed evidence of both deficiencies; and only eighteen, or 3.6 per cent, had neither deficiency. When all four deficiencies are considered for the 425 children with both eye examinations and blood analyses, only four (all boys) were free of any deficiency. The frequency of various combinations of deficiencies is shown in Table 4. Since there were few persons with low hemoglobin, there could be very few who had all four deficiencies, but it is interesting that four of the eight girls who were deficient in iron were also deficient in the three vitamins. The percentage for three deficiency cases was 36.0 among boys and this was 50 per cent higher than the prevalence of three deficiency cases among girls. Conversely, 22 per cent of the girls and 13 per cent of the boys had a single deficiency.

Prevalence of Specific Deficiencies Among WPA Employes

The percentages of employes of the WPA who showed specific deficiencies are given in Table 5. This group had an age range of 17 to 65 years, but the great majority were between 25 and 50 years of age.

Conjunctival change indicative of avitaminosis A was observed

Table 5. Prevalence of four nutritional deficiencies among adults employed by WPA.

Classification of Findings	Percentage of Total			Number Examined		
	Both Sexes	Males	Females	Both Sexes	Males	Females
	Xerosis conjunctivae—avitaminosis A					
Total	100.0	100.0	100.0	143	99	44
Spot Case	45.5	52.5	29.5	65	52	13
Opacity	31.5	30.3	34.1	45	30	15
Marked Translucency						
3–4 Zones	14.0	10.1	22.7	20	10	10
1–2 Zones	8.4	7.1	11.4	12	7	5
No Marked Translucency	0.7	0	2.3	1	0	1
	Keratitis—ariboflavinosis					
Total	100.0	100.0	100.0	138	92	46
Vessels in Cornea	38.4	37.0	41.3	53	34	19
No Corneal Invasion	61.6	63.0	58.7	85	58	27
	Ascorbic acid in plasma					
Total	100.0	100.0	100.0	165	104	61
0.00–0.39 mg. %	39.4	49.0	23.0	65	51	14
0.40–0.59 mg. %	15.8	16.3	14.8	26	17	9
0.60–0.99 mg. %	24.2	24.0	24.6	40	25	15
1.00 or More mg. %	20.6	10.6	37.7	34	11	23
	Hemoglobin level					
Total	100.0	100.0	100.0	138	79	59
10.0–11.9 gms.	3.6	1.3	6.8	5	1	4
12.0–13.9 gms.	30.4	6.3	62.7	42	5	37
14.0 or More	65.9	92.4	30.5	91	73	18

in 142 of 143 persons examined with a slit lamp. The more advanced changes, classified as "spots," were observed in sixty-five, or 45.5 per cent, of the group. This may be compared with 7.7 per cent of "spot cases" among the high school pupils in the low-income group, and it is evident that the adult group was much more seriously deficient in vitamin A. The prevalence of "spot" cases among the men was nearly eighty per cent higher than among the women.

Slit-lamp examination for keratitis of 138 persons showed that 38.4 per cent had a riboflavin deficiency. There was no significant difference in the prevalence for men and women. The records for this group did not permit classification of the stage of keratitis comparable to that used for the high school group; but the total prevalence of 38.4 per cent is only slightly more than one-half that found in the low-income group of high school pupils.

Plasma ascorbic acid levels were less than 0.60 mg. per cent for ninety-one of 165 adults, or 55.2 per cent. As in the high school groups, low ascorbic acid values were more prevalent among men than among women, 65.3 per cent as against 37.8 per cent.

A hemoglobin level below standard was the least frequent deficiency observed among this adult group, but it was somewhat more prevalent than among either of the two high school groups. Among the women, 6.8 per cent had less than 12.0 grams of hemoglobin per 100 cc. of blood, and 7.6 per cent of men had values below 14.0 grams.

Multiple deficiencies must have been common among these adults. Since the prevalence of avitaminosis A was nearly 100 per cent, the majority must have been deficient also in riboflavin or vitamin C.

References

1. Kruse, H. D.; Palmer, C. E.; Schmidt, W.; and Wiehl, Dorothy G.: Medical Evaluation of Nutritional Status. I. Methods Used in a Survey of High School Students. The Milbank Memorial Fund *Quarterly*, July, 1940, xviii, No. 3, pp. 257-283.

2. Kruse, H. D.: Medical Evaluation of Nutritional Status. IV. The Ocular Manifesta-

tions of Avitaminosis A, With Especial Consideration of the Detection of Early Changes by Biomicroscopy. The Milbank Memorial Fund *Quarterly*, July, 1941, xix, No. 3, pp. 207-240.

3. Kruse, H. D.; Sydenstricker, V. P.; Sebrell, W. H.; and Cleckley, H. M.: Ocular Manifestations of Ariboflavinosis. *Public Health Reports*, January 26, 1940, 55, No. 4, pp. 157-169.

4. Sydenstricker, V. P.; Sebrell, W. H.; Cleckley, H. M.; and Kruse, H. D.: The Ocular Manifestations of Ariboflavinosis. *The Journal of the American Medical Association*, June 22, 1940, 114, pp. 2437-2445.

5. Evelyn, K. A.: A Stabilized Photoelectric Colorimeter with Light Filters. *Journal of Biological Chemistry*, August, 1936, 115, pp. 63-75.

6. Mindlin, R. L. and Butler, A. M.: The Determination of Ascorbic Acid in Plasma; a Macromethod and Micromethod. *Journal of Biological Chemistry*, February, 1938, 122, pp. 673-686.

7. Wiehl, Dorothy G.: Medical Evaluation of Nutritional Status. III. Hemoglobin and Erythrocyte Values for Adolescents in High-Income Families. The Milbank Memorial Fund *Quarterly*, January, 1941, xix, No. 1, pp. 45-71.

MEDICAL EVALUATION OF NUTRITIONAL STATUS[1]

VI. DARK ADAPTATION OF HIGH SCHOOL CHILDREN AT DIFFERENT INCOME LEVELS

ELEANOR P. HUNT

INTRODUCTION

DARK adaptation measurements have been widely used to detect night blindness which may be an ocular expression of an avitaminosis A. The term, night blindness, means impaired vision under dim illumination. Its sign is a relative visual failure evidenced by an elevated threshold at light intensities which although low are within the normal range of human visibility.

A variety of factors has been found to alter visual sensitivity. Threshold elevation accompanying lack of vitamin A in the diet or its faulty utilization has been found experimentally in a number of subjects (31, 9, 10, 2, 1). Stewart reported reduction of threshold level by vitamin C therapy (29). Visual sensitivity is reduced by depression of the oxidative process in the central nervous system in anoxia and hypoglycemia (18). Elevated threshold may result also from hereditary abnormality of the retinal rods and ocular pathologies such as opacities of the cornea and lens and lesions of the retina, choroid, and optic nerve (16).

Night blindness due to lack of vitamin A appears to be correlated not only with intraretinal changes but also with changes in the intermediary and central parts of the visual apparatus and central nervous system. Fridericia and Holm (6), Tansley (30), and many later investigators have stressed the association of night blindness during avitaminosis A with reduced regeneration of photo-

[1] This paper is the sixth of a series from a cooperative investigation by the Milbank Memorial Fund; the New York City Department of Health; the United States Public Health Service, Division of Public Health Methods; and the Cornell University Medical College, Department of Public Health and Preventive Medicine and Department of Pediatrics.

The cooperating agencies have been assisted in carrying out this investigation by the Work Projects Administration for the City of New York, Official Project No. 65-1-97-21 W. P. 24, "Medical Evaluation of Nutritional Status."

sensitive pigment in the retina. Recently Moore and Sykes (21), have described the correlation of cerebrospinal fluid pressure with night blindness and papilloedema in calves on a vitamin A deficient diet. Night blindness followed by papilloedema was preceded by an increase in cerebrospinal fluid pressure. Richards and Irving (25) reported very early lesions due to vitamin A deficiency in the optic tract and medulla in rats which were gaining in weight and showed no outward signs of avitaminosis A. It appears from these reports and others that night blindness in avitaminosis A cannot be entirely explained on the basis of photochemistry of the receptor cells and that a broader interpretation is required which takes cognizance of correlated events in extraretinal parts of the visual apparatus and in the central nervous system. Crozier (3, 4) has recently proposed a theory of visual threshold based upon neural units and their fluctuating variation in potential excitability. Night blindness due to vitamin A deficiency, according to Crozier, represents incipient neural injury in the form of a reduced capacity for excitation.

In the present study, children who had no apparent impairment of health were examined. Two socio-economic levels were represented. As part of an attempt to answer the question, what constitutes an elevated threshold, the socio-economic groups are compared with respect to adaptation, diets, and body measurements in the present report. The adaptation performance of the more favorably situated group is also described in detail to provide a reference relative to which unusual values for an individual within the age range of this study can be identified, if test conditions are the same.

Materials and Method

The Sample. The individuals examined were children attending school regularly and taking part also in extra-curricular activities. As judged by these functional criteria, the sample represented a group who had no apparent impairment of health. No gross opaci-

ties or abnormalities interfering with the transmission of light to the retina were reported in the medical examinations by the physician. Refractive anomalies were not measured and have not been corrected for the purpose of the dark adaptation test.

Children of families at a relatively high-income level were examined at a private high school in a semi-suburban locality adjacent to New York City. Children of families at a much lower income level were examined at a public high school on the lower East Side of Manhattan, New York. At both schools the children examined were those willing to participate in the study. In the high-income group, the children were with few exceptions of Jewish parents, born in the United States. In the low-income group most of the children were of Jewish parentage; about 17 per cent were from Italian families. In the majority of cases in the low-income group one or both parents were foreign-born.

Apparatus, Procedure of the Adaptation Test, and Other Observations. One adaptometer constructed according to the specifications of Hecht and Shlaer (11), and purchased in the commercial market[2] was used for all tests described in this report except those of seventy-two cases examined with a different one. The calibrations of the Corning 511 violet filters, the glass wedges, and "neutral" filters were checked by the National Bureau of Standards. The Macbeth Illuminometer was used to calibrate the light source. The instrument was operated in a suitable dark room. The test conditions were those previously employed in the cooperative nutrition study (12). For ease of reference the more important points will be summarized here.

Dark adaptation was preceded by three minutes light adaptation in the brightness range, 12.024-12.052 log $\mu\mu l$ in the case of the instrument used regularly. The preadaptation brightness of the second adaptometer with which seventy-two cases were tested was 11.793 log units. The test

[2] The adaptometer is constructed by O. C. Rudolph, 55 Van Dam Street, New York, N. Y.

field occupied 3 degrees visual angle in diameter. Light adapting and test fields were viewed 7 degrees nasally, using the right eye. The test light was exposed in flashes whose duration was .2 second. A Corning 511 violet filter, which transmitted wave lengths below 460 millicrons, was used during threshold determinations. The brightness of the threshold was expressed in the logarithm of micromicrolamberts ($\mu\mu l$). The dark adaptation period was 30-40 minutes, during which threshold determinations were made at intervals of 2-4 minutes. The method of determining the threshold has been fully described elsewhere (12). The measurements were made by laboratory technicians each of whom had previously examined about 200 subjects.

Preceding the dark adaptation test each subject had a physical examination including observations on the condition of the eyes. The lids, conjunctivae, and pupils were examined for evidence of obvious infection. Movement was tested. The Snellen test of visual acuity was made routinely.

Diet histories were obtained by interview. The kind and amount of foods and mixed dishes eaten in a two-day period immediately preceding the day of the interview were recorded.[8]

Anthropometric measurements were taken either on the day of the dark adaptation test or within a short interval.

Statistical Procedure. Threshold measurements of children in each income group were described by the statistical measures commonly employed to examine and summarize other psycho-physi-

[8] The commercial name or the brand or type of each food was obtained whenever possible together with a description of the manner in which the food was prepared. The child was questioned with regard to the composition of any mixed dishes reported, such as soup, stew, salads, and sandwiches and concerning the use of sugar, cream, butter, gravy, etc., with any of the foods or mixed dishes eaten. Quantity eaten was estimated relative to standard measure; cup, glass (large or small), teaspoon, tablespoon, sauce dish, which were available for display, or by reference to artificial casts of standard servings of frequently used mixed dishes. The enumeration included items eaten between meals and vitamin and mineral concentrates. Habits with respect to the frequency of use of protective foods, such as milk, eggs, fruits, and vegetables, were recorded. The child was questioned regarding types of activity, and their duration during the forty-eight hour period covered by the diet history. Over 500 recipes for mixed dishes frequently served were collected in the field and in the schools concerned to check upon the composition of mixed dishes reported by children. The approximate size of servings of various foods and mixed dishes used in the school lunches was also determined.

ological observations. At a given minute in the dark the set of threshold values obtained for all of the individuals concerned formed a frequency distribution characterized by clustering at a central value and dispersion in opposite directions.

With regard to early and late adaptation the frequency distributions of threshold at single minutes were found to be fairly symmetrical and to resemble the normal type. The ogives of threshold distributions before 5 minutes and after 9 minutes were found to be sufficiently rectified by a probability grid to justify the use of the mean and standard deviation to describe such distributions.

In the neighborhood of 5-9 minutes of adaptation, the frequency distributions of threshold were less symmetrical. In this period a strong skewed effect was evident and percentiles (the 90th, 75th, 50th, 25th, 10th) as well as the mean and standard deviation, have been relied upon to indicate levels of threshold above which were found the percentage of cases stipulated.

Subjects concerned in the present report were classified according to certain factors which were found to cause significant variation in threshold level. Thus, a preliminary analysis of results in 267 cases available early in the study showed that when the entire course of adaptation was to be considered, the subjects must be grouped according to income level, brightness of preadaptation, and the different technicians making the tests. If only the threshold later than 20 minutes were considered groupings were needed according to income and technician. At that time preadaptation differences were no longer significant (12).

Effects upon the mean or variance of threshold after 20 minutes, which might be due to a number of other factors, were also evaluated in the preliminary analysis of the results for 267 cases. Classifications for age, sex, acuity as measured by the Snellen test, pigmentation of the iris, hour of the test, time of color change from purple, violet, or blue to gray or white and phase of the menstrual cycle gave no evidence in a covariance analysis of differences in

mean adjusted threshold after 20 minutes which could not be accounted for by chance.[4]

Adaptation at Different Income Levels

The mean threshold for children in the low-income group tended to be higher throughout adaptation than the mean for the high-income group. The difference was greater after 20 minutes of adaptation than at earlier times. Merging or crossing of the mean threshold levels were relatively infrequent and occurred before 20 minutes when adaptation was rapid and observational errors tend to be greater (12). Some uncertainty in the comparison resulted also from the small number of children involved and the fact that not every child could be examined at each minute. If these limitations are borne in mind, the mean performance of the two groups would appear to differ significantly before 20 minutes and in a manner consistent with the larger differences after 20 minutes.

Mean threshold intensity during adaptation for children in the high and low-income groups is shown in Table 1 and the corresponding Figure 1 in which threshold intensity (log $\mu\mu l$) is plotted against dark time.[5] All cases included in Table 1 were examined by one technician. The sixty-four cases of the high-income group were preadapted to 1,060, those of the low-income group to 1,080 millilamberts, a difference which would not account for the progressive differences in mean threshold level shown in Figure 1.

Larger subsamples of children at the two income levels indicated that the mean adaptation of the low-income group was not only slower but also more variable at corresponding dark times. The larger subsamples of children were obtained for the two income groups by combining 175 cases following 1,060 millilamberts pre-

[4] In testing the null hypothesis regarding sample means or variances the "F" distribution (27) has been used. In some instances Student's "t" was employed to test significance of mean difference (5). For either criterion, $p. \leq .01$ was taken as the level of statistical significance.

[5] The time (minutes) elapsed after light adaptation and during dark adaptation.

Time in the Dark	Threshold[1]					
	High-Income Group—64 Cases			Low-Income Group—98 Cases		
	Observations	Mean	Standard Error	Observations	Mean	Standard Error
(Minutes)	(Number)	(Log $\mu\mu l$)	(Log $\mu\mu l$)	(Number)	(Log $\mu\mu l$)	(Log $\mu\mu l$)
0.5	63	6.372	±.014	98	6.460	±.014
1.5	1	6.059	—	—	—	—
2.5	57	5.844	±.021	81	5.887	±.016
3.5	5	5.784	±.065	17	5.900	±.048
4.5	31	5.576	±.021	16	5.596	±.036
5.5	32	5.416	±.037	78	5.521	±.020
6.5	21	5.283	±.028	7	5.375	±.202
7.5	28	4.990	±.093	42	5.158	±.076
8.5	13	4.547	±.182	41	4.475	±.077
10.0	38	4.051	±.030	21	4.202	±.054
11.0	17	3.905	±.098	41	4.046	±.063
12.0	8	3.952	±.217	31	3.847	±.040
13.0	33	3.626	±.035	15	3.718	±.057
14.0	19	3.436	±.041	31	3.656	±.044
15.0	13	3.375	±.112	45	3.474	±.038
16.0	28	3.278	±.039	15	3.408	±.035
17.0	24	3.176	±.030	29	3.326	±.035
18.0	5	2.954	±.105	34	3.245	±.034
19.0	25	3.065	±.054	25	3.125	±.049
20.0	27	2.960	±.034	28	3.118	±.039
21.0	11	2.866	±.064	22	3.111	±.036
22.0	23	2.799	±.056	39	3.019	±.028
23.0	26	2.706	±.036	20	2.871	±.046
24.0	15	2.712	±.065	35	2.978	±.032
25.0	15	2.640	±.052	34	2.859	±.024
26.0	28	2.569	±.037	15	2.891	±.066
27.0	19	2.560	±.031	35	2.810	±.034
28.0	15	2.512	±.044	31	2.803	±.033
29.0	24	2.455	±.020	24	2.797	±.034
30.0	21	2.478	±.114	35	2.700	±.039
31.0	14	2.450	±.097	33	2.726	±.034
32.0	25	2.414	±.030	20	2.726	±.054
33.0	20	2.430	±.035	21	2.652	±.050
34.0	19	2.440	±.037	39	2.655	±.037
35.0	18	2.387	±.016	26	2.655	±.043

[1] The observations were grouped in one minute intervals centered on the half minute before 9 minutes of adaptation and on the whole minute after 9.5 minutes, a procedure which followed the observed clustering of the data.

Table 1. Mean threshold and standard error, according to time in the dark, for children in the high and low-income groups who were preadapted to 1,060 millilamberts and 1,080 millilamberts respectively with one adaptometer by a single technician.

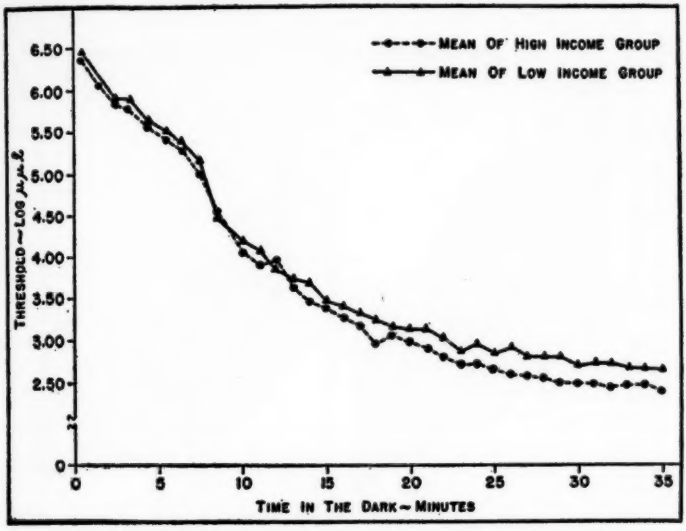

Fig. 1. Mean threshold during dark adaptation for children in the high-income group and in the low-income group, following 3 minutes preadaptation to 1,060 and 1,080 millilamberts, respectively.

adaptation tested by four technicians in the high-income group and by combining in the low-income group 240 cases tested by one of the same technicians and preadapted in the brightness range 1,117-1,127 millilamberts.

The greater number of technicians testing in the high-income group would tend to augment rather than decrease the variability of results in that group. The maximum difference in preadaptation (67 millilamberts) between the income groups, as represented in these subsamples, was insufficient to cause significant differences in mean threshold level or in variability after 20 minutes adaptation. Therefore, the comparison between income groups with respect to variability in adaptation performance has been made for thresholds after 20 minutes adaptation.

In Figure 2 the dispersion of threshold values after 20 minutes is illustrated for the two income groups by means of selected per-

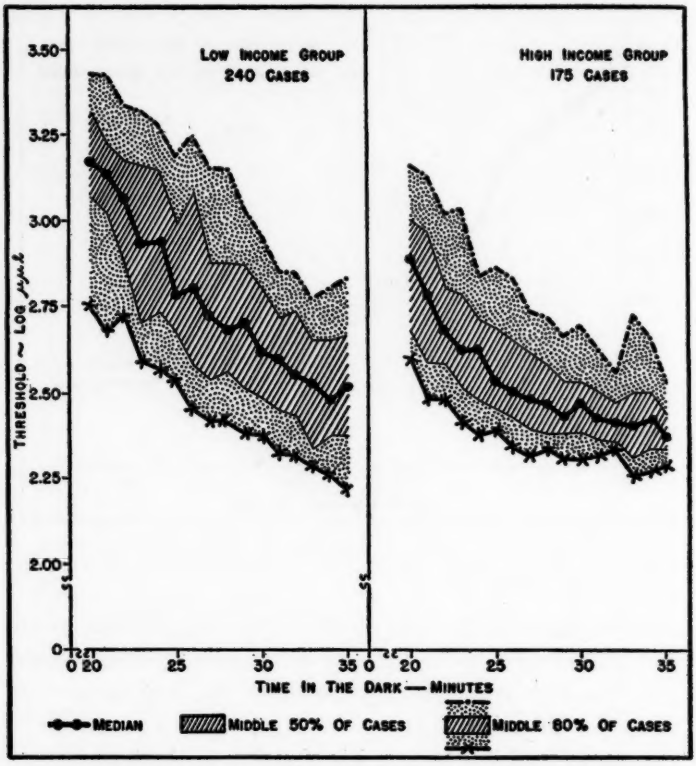

Fig. 2. Adaptation contours after 20 minutes in the dark for children in the high-income and in the low-income group following 3 minutes preadaptation to 1,060 and 1,080 millilamberts, respectively.

centiles of the frequency distributions of threshold at successive minutes. The adaptation contours so described showed quite different dispersions. At corresponding times the variability of the low-income group was greater throughout the interval, 20-35 minutes, and distributed about a higher median threshold level. In the high-income group the variability declined during 20-35 minutes more rapidly than in the low-income group. The relatively reduced variability expected toward the end of adaptation was found in the

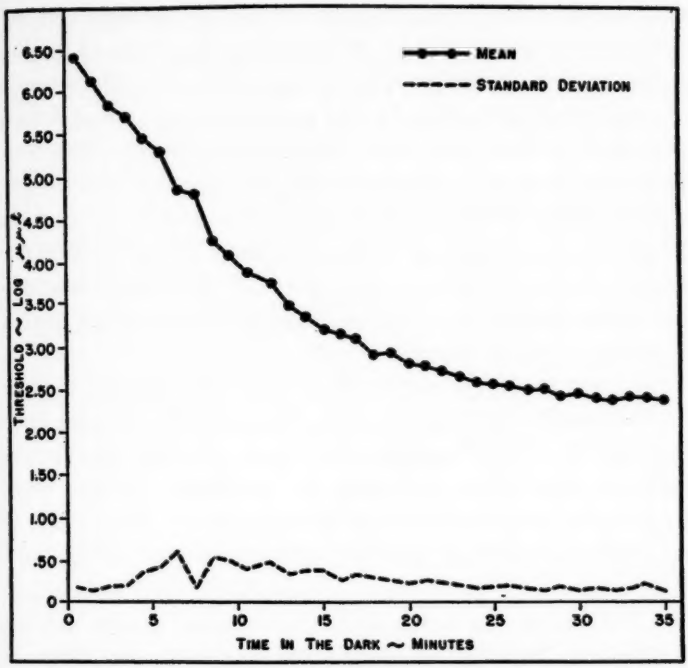

Fig. 3. Mean and variability of threshold during dark adaptation for 175 children of the high-income group examined by four technicians following 3 minutes pre-adaptation to 1,060 millilamberts.

high-income group by 35 minutes. At 30 minutes and later in the low-income group the variability was as great as that of the high-income group at 20 minutes.

The evidence of higher mean threshold and greater variability of the low-income group, shown in Figures 1 and 2, was supported by the results of the preliminary analysis for 267 cases referred to under statistical procedures. The preliminary analysis included the work of one technician at the public and private schools, which had been completed during one school year when the analysis was begun. The data covered sixty-four children of the 175 high-income cases whose results are shown in Figure 3 and seventy-two other

high-income cases examined on the second adaptometer and not included in Figure 3 because their preadaptation was 11.793 log units as compared with 12.024 for the cases of Figure 3. The seventy-two cases could be included in the preliminary analysis in which preadaptation differences were controlled statistically. The low-income cases of the preliminary analysis were the ninety-eight children whose test results appear in Table 1 and thirty-three additional cases not included in Table 1 because of a preadaptation difference. In this analysis there were five or six threshold determinations for each subject after 20 minutes adaptation making a total of 1,579 observations for the 267 subjects.

The mean threshold level for the entire set of 1,579 observations after 20 minutes was 2.653 log units. The variability between cases measured by errors of estimate after linear regression was ± .421 log units. This figure represents the variability between mean thresholds of individual children after 20 minutes, independent of any small differences in mean observation time, and which were alike with respect to income, preadaptation, and technician.[6] Threshold values for the high and low-income groups differed significantly. The mean threshold levels after 20 minutes, adjusted to average observation time were 2.540 log units and 2.765 log units for the high and low-income groups respectively. The variability between cases (errors of estimate) for the high-income group was ± .330 log units and considerably greater for the low-income groups, ± .516 log units.

Threshold Characteristics of the High-Income Group. The test results throughout adaptation for the 175 cases of the high-income group are of interest as an indication of expected performance of an urban population of mixed bio-ethnic origin, not handicapped by unfavorable socio-economic circumstances. The tests were made by several experienced technicians and should therefore provide a

[6] The corresponding variance was .177 log units[2] associated with 245 degrees of freedom. This variance was used as "error" in the preliminary analysis.

more general description of adaptation results than can be obtained on the basis of a single technician. Inasmuch as adaptation measurements in different studies must usually be made by different tech-

Table 2. Mean, standard deviation, and standard error of threshold for 175 children of the high-income group after preadaptation for 3 minutes to 1,060 millilamberts, according to time in the dark.

Time in the Dark	Observations	Threshold		
		Mean	Standard Deviation	Standard Error
(Minutes)	(Number)	(Log $\mu\mu l$)	(Log $\mu\mu l$)	(Log $\mu\mu l$)
0.5	172	6.436	±.187	±.014
1.5	3	6.145	±.149	±.086
2.5	157	5.847	±.198	±.016
3.5	15	5.722	±.219	±.056
4.5	105	5.473	±.360	±.035
5.5	59	5.323	±.445	±.058
6.5	79	4.851	±.614	±.069
7.5	66	4.828	±.176	±.022
8.5	66	4.259	±.554	±.068
9.5	55	4.088	±.496	±.067
10.5	76	3.879	±.397	±.046
12.0	53	3.748	±.479	±.066
13.0	85	3.479	±.345	±.012
14.0	63	3.352	±.384	±.048
15.0	46	3.218	±.381	±.056
16.0	78	3.181	±.282	±.032
17.0	56	3.100	±.342	±.046
18.0	49	2.902	±.313	±.045
19.0	61	2.936	±.284	±.036
20.0	54	2.831	±.242	±.033
21.0	48	2.779	±.250	±.036
22.0	51	2.714	±.241	±.034
23.0	56	2.656	±.219	±.029
24.0	56	2.607	±.194	±.026
25.0	51	2.597	±.184	±.026
26.0	58	2.552	±.193	±.025
27.0	55	2.508	±.169	±.023
28.0	50	2.511	±.159	±.023
29.0	59	2.457	±.180	±.023
30.0	56	2.463	±.154	±.021
31.0	48	2.436	±.160	±.023
32.0	51	2.409	±.151	±.021
33.0	50	2.445	±.172	±.024
34.0	58	2.423	±.220	±.029
35.0	50	2.398	±.127	±.018

nicians a general description which includes technician peculiarities is a safer reference in comparisons than one which is limited to a single observer, provided that the several technicians are competent.

No definite specifications can be given with regard to the vitamin A nutrition of the high-income group. No doubt numerous individuals were included whose vitamin A nutrition was not optimal. Identification of such cases can be made only by subsequent and suitable experiment. The sample was not, therefore, representative of a well-nourished population in a strict sense.

Threshold Distributions During Adaptation. Mean threshold, standard deviation, and standard error are given for the 175 cases of the high-income groups in Table 2 for each minute up to 36 minutes dark time. The mean threshold at 30 minutes was 2.463 log units and the standard deviation, .154 log units. In the neighborhood of 30 minutes dark time the entire range of thresholds observed was approximately 1.0 log unit. The variability of threshold increased rapidly during the first 7 minutes of the test, at which time it apparently reached a maximum and then declined, reaching at 25 minutes values comparable to those obtained immediately after preadaptation. The fluctuation of the standard deviation is closely correlated with observational error, which in turn is associated with rate of adaptation. The larger standard deviations in the interval, 5-10 minutes, also reflected differences among the 175 cases with respect to onset of secondary or "rod" adaptation. Figure 3 illustrates the regression of mean threshold and the variability.

The frequency percentage distributions of threshold at 0.5, 4.5, 8.5, 13.0, 17.0, 21.0, 25.0, 29.0, and 33.0 minutes are shown in Figure 4. Greater concentration of values was evident early and late in adaptation and marked skewed effects in the same direction were obtained at 8.5 minutes and at 25, 29, and 33 minutes.

Several percentiles were used to illustrate more clearly the change in form of the successive distributions. The threshold values corres-

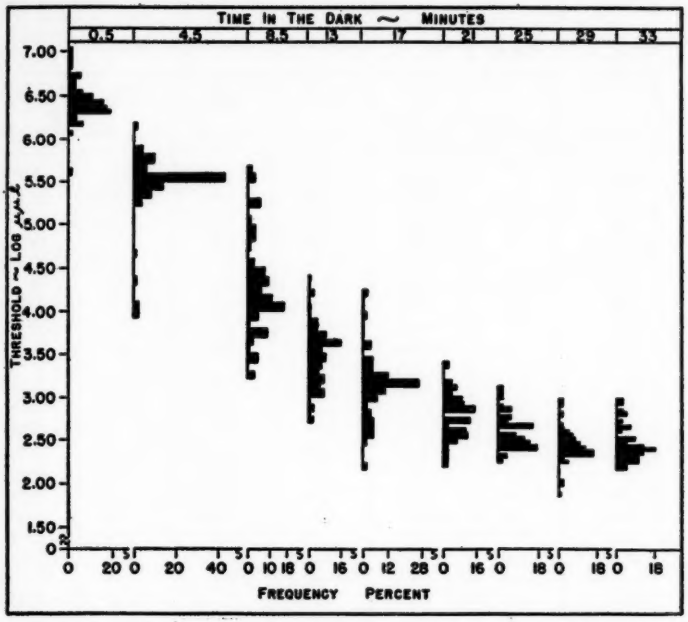

Fig. 4. Frequency percentage distributions of threshold at specified times during dark adaptation for 175 children of the high-income group examined by four technicians, following 3 minutes preadaptation to 1,060 millilamberts.

ponding to the several percentiles were interpolated from the distribution at each minute, except at 1.5 minutes and between 11-11.5 minutes when only a few cases were observed. The percentile values are given in Table 3. Figure 5 shows the adaptation contour for the middle 80 per cent and middle 50 per cent of cases up to 36 minutes.

The adaptation of the middle 50 per cent appeared to be complete at about 30 minutes. Before 6 minutes and after 10 minutes the middle 50 per cent of cases were distributed symmetrically about the median. Owing to differences among individuals with respect to time of maximum rate of adaptation skewed effects in opposite directions occurred immediately preceding and following the 7.5 minute point. Judged by the median the maximum rate of adapta-

Time in the Dark	Observations	Threshold at Specified Percentiles				
		90th	75th	50th	25th	10th
(Minutes)	(Number)	(Log $\mu\mu l$)	(Log $\mu\mu l$)	(Log $\mu\mu l$)	(Log $\mu\mu l$)	(Log $\mu\mu l$)
0.5	172	6.68	6.50	6.40	6.33	6.23
2.5	157	6.08	5.98	5.87	5.73	5.55
4.5	105	5.77	5.60	5.54	5.45	5.30
5.5	59	5.75	5.58	5.39	5.24	4.69
6.5	79	5.54	5.30	5.20	4.32	4.06
7.5	66	5.38	5.27	5.18	4.28	3.95
8.5	66	5.21	4.47	4.15	3.96	3.65
9.5	55	4.78	4.34	4.11	3.78	3.38
10.5	76	4.30	4.17	3.90	3.67	3.31
12.0	53	4.28	3.99	3.64	3.46	3.26
13.0	85	3.86	3.69	3.51	3.21	3.05
14.0	63	3.68	3.50	3.35	3.13	2.91
15.0	46	3.63	3.46	3.20	2.99	2.70
16.0	78	3.50	3.36	3.19	2.95	2.83
17.0	56	3.43	3.26	3.14	2.91	2.62
18.0	49	3.33	3.09	2.90	2.68	2.51
19.0	61	3.23	3.11	2.93	2.72	2.56
20.0	54	3.16	3.00	2.89	2.68	2.60
21.0	48	3.14	2.97	2.78	2.59	2.48
22.0	51	3.02	2.80	2.69	2.58	2.48
23.0	56	3.03	2.79	2.63	2.51	2.41
24.0	56	2.83	2.71	2.62	2.47	2.37
25.0	57	2.86	2.69	2.53	2.45	2.39
26.0	58	2.83	2.65	2.50	2.42	2.33
27.0	55	2.73	2.61	2.48	2.39	2.31
28.0	50	2.71	2.58	2.47	2.38	2.33
29.0	59	2.66	2.53	2.43	2.37	2.30
30.0	56	2.69	2.53	2.47	2.38	2.30
31.0	48	2.60	2.50	2.42	2.36	2.31
32.0	51	2.55	2.47	2.41	2.35	2.33
33 0	50	2.72	2.50	2.40	2.30	2.25
34.0	58	2.66	2.50	2.42	2.33	2.26
35.0	50	2.53	2.43	2.37	2.33	2.28

Table 3. Threshold, at specified percentiles of the frequency distributions for the 175 cases of the high-income group who were preadapted for 3 minutes to 1,060 millilamberts, according to dark time.

tion occurred just about 7.5 minutes. After 20 minutes the percentiles above the 75th departed progressively toward higher threshold values.

Correlation between Threshold Early and Late in Adaptation.

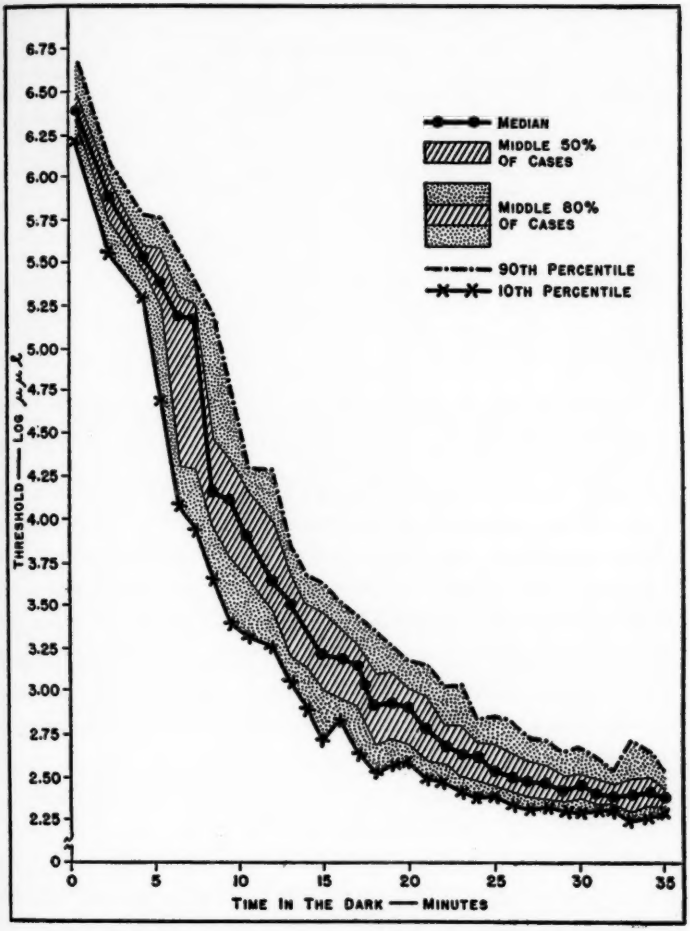

Fig. 5. Dark adaptation contour for 175 children of the high-income group who were examined by four technicians and preadapted for 3 minutes to 1,060 millilamberts.

The correlation between mean threshold at 30-35 minutes and thresholds obtained earlier in adaptation indicated that the rank order of a child early in the test was not a dependable indication of

Time in the Dark	Observations	Coefficient of Correlation (r)	Standard Error of Estimate (s y.x.)	Regression Coefficient (b)	Variation in Threshold Accounted for by Regression ($r^2 \times 100$)
(Minutes)	(Number)	(Number)	(Log $\mu\mu l$)	(Number)	(Per Cent)
2.5	155	+.0924	±.194	+ .127	0.8
4.5	104	−.0192	±.360	− .048	0.0
10.0	82	−.0203	±.398	− .057	0.0
13.0	85	+.1058	±.344	+ .262	1.1
16.0	78	+.3587	±.284	+ .952	12.9
18.0	47	+.4127	±.295	+ .912	17.0
24.0	54	+.4949	±.172	+ .703	24.5
26.0	58	+.8593	±.099	+1.057	73.8
29.0	58	+.9314	±.067	+ .825	86.8

Table 4. Correlation statistics for mean threshold after 30-35 minutes dark adaptation and threshold after specified shorter periods of adaptation, following 3 minutes preadaptation to 1,060 millilamberts.

his rank for mean threshold at 30-35 minutes. Summarized in Table 4 are coefficients of correlation and related statistics for mean threshold at 30-35 minutes and threshold determined at each of nine other dark times. The coefficient of correlation was not significant until 16 minutes when the value was + .35. Not until 26 minutes was the relationship to the mean threshold at 30-35 minutes sufficiently close to be of practical importance. The change from fairly close relationship at 26 and 29 minutes to independence before 16 minutes is shown in Figure 6.

Diets and Body Measurements of Children in the High and Low-Income Groups

The diets and body measurements of the high and low-income groups are of interest in view of the known association of threshold elevation with nutrition and the relation of the latter to growth of the body. At this time diet descriptions can be given for the 267 children of the high and low-income groups shown by the preliminary analysis to differ significantly with respect to adjusted mean threshold level after 20 minutes adaptation and with respect to variability of adaptation as well. There were in this subsample

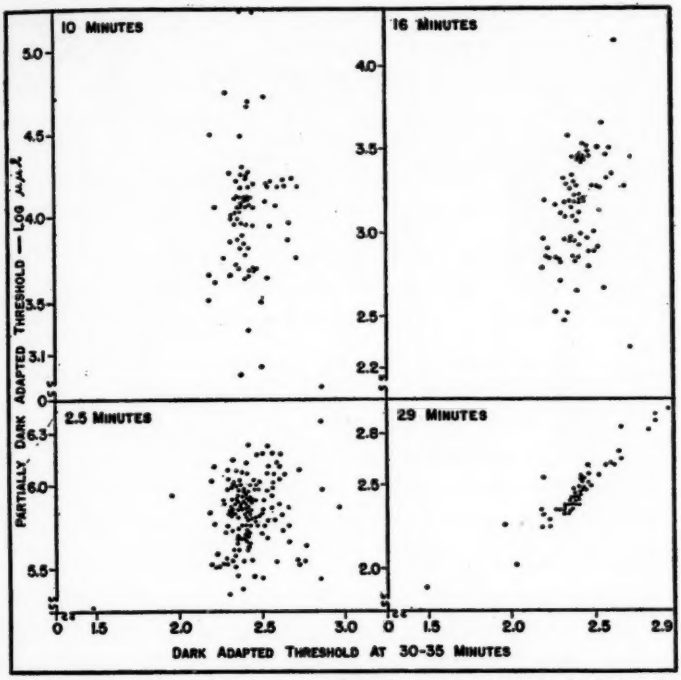

Fig. 6. Correlation of the mean threshold after 30-35 minutes in the dark and partially dark adapted thresholds following preadaptation for 3 minutes to 1,060 millilamberts.

136 children of the high-income group and 131 children of the low-income group. It is believed that the present diet descriptions although limited to 267 children are representative of the dietaries characteristic of persons in the two income groups whose adaptation is described. A full analysis and discussion of the diets will be given in other reports. Comparison of body development of the children in the two income groups was made on the basis of the full sample of children examined at each income level in the nutrition study. It was found that the stature, weight, and age distributions of the cases whose adaptation and diets are described did not differ significantly from those of the respective samples.

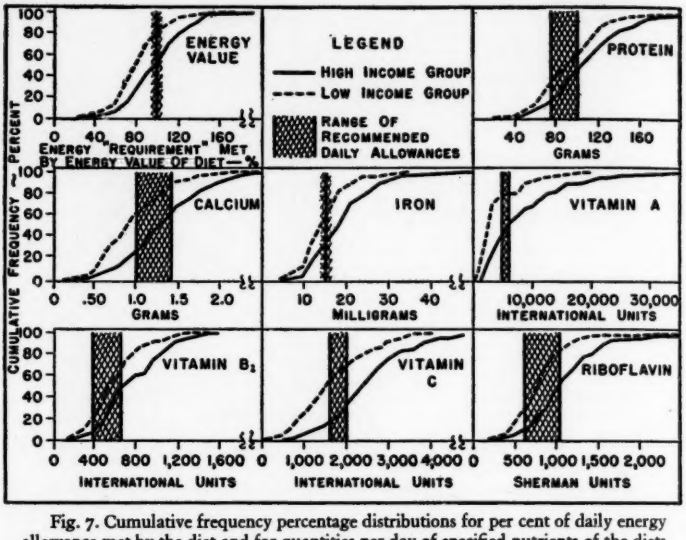

Fig. 7. Cumulative frequency percentage distributions for per cent of daily energy allowance met by the diet and for quantities per day of specified nutrients of the diets of 136 children of the high-income group and 131 children of the low-income group.

Nutritive Content of the Diets. The estimates of nutritive content are subject to the uncertainties inherent in the interview method and in the application in particular cases of average values for food composition. The procedure of interview was uniform in the two income groups and it is likely that the relative position of the groups is reflected approximately although the estimates of nutritive content may not correspond exactly with those which would be obtained by another method.

Recommended daily allowances of different nutrients serve as a rough yardstick to indicate dietary "adequacy" from the point of view of practice tentatively regarded as desirable. In Figure 7, a recommended range or level of daily allowance is shown for protein; calcium; iron; and vitamins A, B, C; and riboflavin.[7] The

[7] The daily allowances indicated graphically are based upon quantities of the specified nutrients which were recommended for boys in the age groups, 13-15 years and 16-20 years, and for girls in the same age groupings (23). With the exception of four 12-year-old

(Continued on page 271)

quantities of the several nutrients provided by the respective diets of the two income groups are compared with the recommended allowances by means of cumulative frequency distributions for each nutrient. In this general comparison sex and age groups have been combined.

In the case of energy value, individual "requirements" per twenty-four hours were computed according to basal caloric "requirements" for age, sex, surface area, and estimates of need for growth and type of activity reported on the child's diet history. The energy value provided by the child's diet as described was then expressed in per cent of the child's "requirement."

Thus in Figure 7, the panel for energy value shows the percentage of children having diets which provide varying proportions (in per cent) of the individual energy "requirement." Regardless of the basis of estimating individual energy requirements Figure 7 indicates that the percentage of diets meeting energy "requirement" in the low-income group was considerably smaller than corresponding percentages of the high-income group.

Large differences occurred with respect to daily vitamin A intake. Approximately 78 per cent of the diets of the children in the low-income group and 44 per cent of the diets in the high-income group were providing less than 5,000 I.U. per day.

With respect to daily intake of protein, vitamins B_1 and riboflavin the diets of the majority of children in both income groups appeared to be satisfactory relative to the tentative and approximate allowances. However, for each of these nutrients the diets of larger percentages of children of the low-income group than the high-income group fell short of recommended daily allowances.

Fifty-two per cent of the children of the low-income group and

boys and six 12-year-old girls, the ages of all children whose diets are discussed in this report were in the age range 13-19 years. In Figure 7 the least quantity recommended in the age groupings, 12-15 years, 16-20 years, for either sex was used as the lower limit of the indicated range of daily allowance. The upper limit corresponds to the largest quantity recommended among the four age-sex groups.

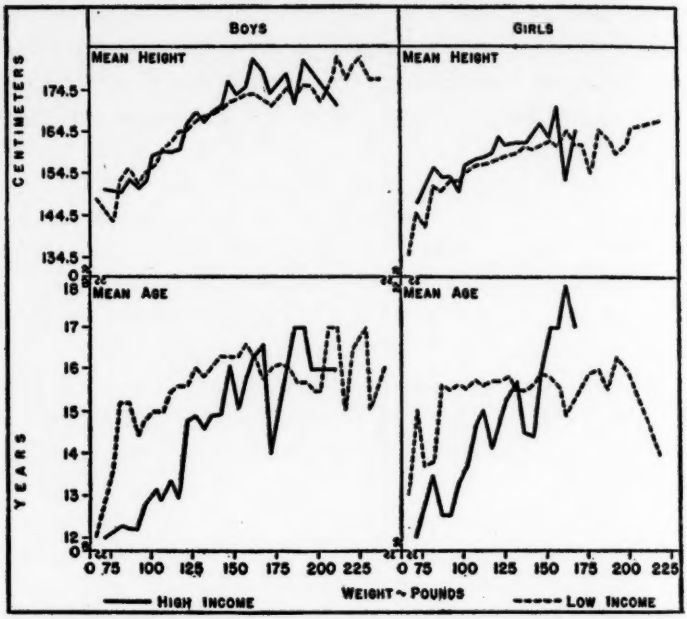

Fig. 8. Mean height and mean age according to weight, for 183 boys and 171 girls of the high-income group and for 1,169 boys and 1,020 girls of the low-income group.

18 per cent of the high-income cases were receiving less than the recommended allowance of vitamin C. Similar percentages of the diets fell below a daily allowance of 1.0 gram of calcium.

Stature, Weight, and Age. Full consideration of differences in body measurements cannot be given here but differences were outlined according to the relationship between stature, weight, and age. For equal weight the children of the low-income group tended to be shorter and older. Mean stature and mean age according to weight are shown in Figure 8. It was found that boys with body weight of less than 162 pounds (86 per cent of low-income classes, 90 per cent of high-income cases) attained equal weight in a shorter mean growth period in the high-income group. Similarly, for girls

with body weight less than 147 pounds (89 per cent of low-income cases, 92 per cent of high-income cases) the mean growth period to reach equal weight was shorter for the high-income group. Mean stature for equal weight and younger age was greater in the high-income group, quite consistently for girls and frequently in the case of boys.

Discussion

In this survey visual sensitivity was found to be correlated with income level. The relationship has been reported also in other studies of apparently well persons. (14, 22, 20, 24, 17.) The difference found here between income groups in mean threshold after 20 minutes was small (.225 log units after 20 minutes), but it tended to increase with dark time. The pattern of difference shown in Figure 2 resembles threshold changes reported as associated with vitamin A deficiency (2, 31, 9), and with reduced oxidation in hypoglycemia (19). The diet descriptions of the respective income groups indicated that the vitamin A intake and energy value of the diets of the low-income group were less satisfactory, relative to recommended daily allowances, than were those of the high-income group. Thus the dietary evidence supported an interpretation that the differences in visual sensitivity of the two groups might be a reflection of different levels of vitamin A intake and differences with respect to available glucose and its metabolism. However, the degree of the relationships between visual sensitivity, vitamin A intake, and glucose metabolism is highly uncertain. In several experiments, human subjects have failed to show threshold elevation when vitamin A was withheld from the diet (28, 13). In the present study, data bearing directly upon the question of differences in capacity to oxidize glucose were not available.

Since changes in visual sensitivity during adaptation following vitamin C therapy have also been reported (29) and the diets of the children of the two income groups concerned here differed

almost as widely with respect to vitamin C as vitamin A, the additional question is raised whether this nutrient may not also have contributed to the different visual response of the two groups. Neither the latter possibility nor the relative roles of vitamin A and glucose metabolism in visual efficiency can be accurately evaluated on the basis of present knowledge.

The income groups showed differences which may be of nutritional origin not only in visual function but also in body development as indicated by stature, weight, and age. The differences in body development were too great to be explained entirely by body build. The fact that in the majority of cases children in the low-income group were shorter for equal weight might be attributed in part to relatively greater cross-sectional growth and skeletal differences. But the greater age for equal weight in addition to shorter stature suggested a retardation in growth.

Night blindness due to vitamin A deficiency is customarily interpreted according to the duplicity theory of vision (26) and the photochemical hypothesis (15, 8). These theories largely disregard the effects upon visual response of nerve, of the central parts of the visual apparatus, and of the central nervous system. The evidence of change in cerebrospinal fluid pressure preceding night blindness and the appearance of very early lesions of the optic tract and medulla in vitamin A deficiency cannot be brought within the framework of a photochemical explanation. Crozier's interpretation of dark adaptation is of interest because, among other reasons, it considers the co-functioning of receptor cells and of intermediary and central parts of the visual mechanism in relation to the central nervous system in general.

Crozier's theory assumes that visual response results from the stimulation by light of excitable neural units which momentarily fluctuate in intensity threshold at random. It is presumed also that during adaptation the neural units vary in capacity to produce nerve impulses when stimulated. In all available series of measurements

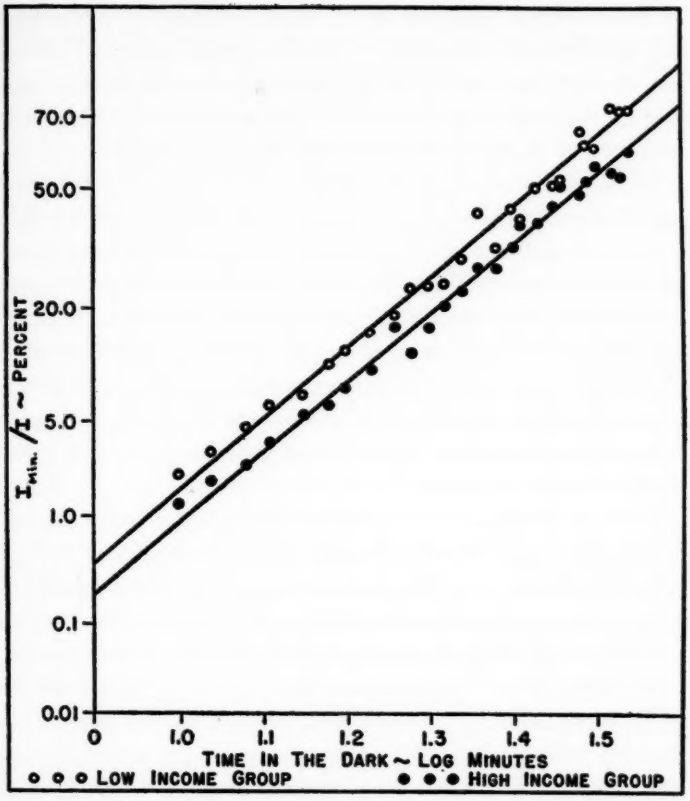

Fig. 9. Mean excitability at successive minutes after 9 minutes dark time, in per cent of maximum mean excitability for ninety-eight children of the low-income group preadapted for 3 minutes to 1,080 millilamberts and for sixty-four children of the high-income group who were preadapted for 3 minutes to 1,060 millilamberts.

of man and of all other animals that have been tested Crozier has shown that threshold during dark adaptation can be expressed by a probability integral as a function of log dark time (3, 4).

The dark adaptation response of the children in the different income groups, described in Table 1, is represented in Figure 9 on a probability grid. The ordinate is the ratio in per cent of the theoreti-

cal minimum threshold intensity (I_{min}) at the end of the adaptation and threshold intensity (I) at each observation time. This ratio ($\frac{I_{min}}{I} \times 100$) is presumed to express excitability ($\frac{1}{I}$) during adaptation in relation to final or maximum excitability, which is the reciprocal of the minimum threshold intensity ($\frac{1}{I_{min}}$).

Considerable scatter of the points is evident and might be expected in view of the fact that means based upon different subjects have been used and case composition fluctuated at successive minutes. The theoretical minimum threshold for the low-income groups was 2.506 log units. The corresponding value for the high-income groups was 2.156 log units. The lower minimum threshold of the high-income group signifies a greater capacity of neural units to produce nerve impulses or neural effects. In Figure 9 the equal slope of the lines may be taken to indicate that comparable groups of neural units are involved.

In school or community surveys of dark adaptation the majority of subjects can be tested only once and performance of the individual is judged according to the expected threshold of subjects who are apparently well and who have been tested under the same conditions. The dark adaptation results in Table 3 for the children of the high-income group indicate the range of threshold values to be expected of the middle 80 per cent of children who are apparently well and in the age range 12-19 years. The percentiles provide a method of describing conveniently the usual threshold values of this group. Despite case fluctuation at successive minutes, selected percentiles after 20 minutes may very well reflect to a considerable extent the threshold level of children who have relatively the highest, the lowest, and the middle threshold values. Usual performance, as shown by the middle 50 per cent of cases, was between 2.68 and 3.00 log units at 20 minutes and between 2.38 log units and 2.53 log units at 30 minutes. The skewness toward higher values of percentiles above the 75th after 20 minutes suggested that children so placed may be unable to complete the final phases of adap-

tation as successfully as the middle 50 per cent which was more symmetrically distributed. Judged according to the threshold distributions of this study, test results which fall consistently above 3.00 log units (75th percentile) after 20 minutes are unusually high and the subjects concerned are worthy of additional study.

Since the visual threshold as measured is a psychometric observation it was thought that the child's general aptitude in school might have some effect upon his test results. The upper and lower 25 per cent of the children ranked according to the adaptation test results, were compared with respect to school behavior, to obtain a preliminary indication of whether such a relationship might be involved. Satisfactory quantitative ratings for school behavior were not available and the opinion of teachers and supervisor was the basis of rating for adjustment in school. The comparison suggested that performance on the test may be related to success in academic work, social adjustments, and emotional stability. A relatively large number of children who were thought to be ill-adjusted in school ranked poorly on the test whereas only a few children so regarded by the school authorities were found among the 25 per cent of children whose adaptation reached the lowest threshold levels. On the basis of this limited comparison the correlation between school behavior and test performance can only be suggested in the form of a question.

Pathogenetic studies of threshold elevation due to vitamin A deficiency have shown in certain cases that thresholds late in adaptation respond to lack of vitamin A sooner and to a greater extent than earlier thresholds. (2, 31, 10). It would appear to be advisable, therefore, to give considerable weight to performance after 30-35 minutes if the object of the observations is an early reflection of avitaminosis A. The negligible correlations between threshold at 30-35 minutes and much earlier thresholds suggest that thresholds before 26 minutes do not give dependable information regarding those of the later stages of adaptation. If the information desired

concerns the relative performance of the individual after 30 minutes adaptation, the threshold should be observed at that time. In serial studies of experimental night blindness and of individuals with cirrhosis of the liver (7) thresholds early and late in adaptation have been found to be more highly correlated than those described here. Subjects in such studies become experienced and the loss of correlation due to observational error is less than in the situation where the subjects are examined only once.

Summary

1. Visual threshold measurements, diets, and body measurements of high school children, 12-19 years of age, at different income levels are described. The threshold measurements were made with the Hecht adaptometer according to specified test conditions.

2. The mean threshold after 20 minutes, for 131 children of the low-income group was 2.765 log units with a variability (errors of estimate) of ± .516 log units. The corresponding values for 136 children in the high-income group were 2.540 log units ± .330 log units.

3. Seventy-eight per cent of the diets of the children in the low-income group and 44 per cent in the high-income group were providing less than 5,000 I.U. vitamin A daily. Larger percentages of the diets in the high-income group than in the low-income group were providing energy value; protein; calcium; vitamins B_1, C; and riboflavin in satisfactory quantities as judged by tentative and approximate allowances recently recommended.

4. The relationships between mean height and mean age with weight constant showed that the majority of children of the high-income group were taller and younger for equal weight than those of the low-income group.

5. Mean threshold level after 20 minutes was not affected in either income group by age, sex, acuity as measured by the Snellen test, pigmentation of the iris, hour of the test, time of color change from

purple, violet, or blue to gray or white, or phase of the menstrual cycle.

6. The mean threshold level at 30 minutes for 175 cases of the high-income group, examined by four technicians and preadapted to 1,060 millilamberts was 2.463 log units with a standard deviation of ± .154 log units. The range at 30 minutes was 1.0 log unit. Judged by the median the maximum rate of adaptation occurred just after 7.5 minutes dark time.

7. Mean threshold at 30-35 minutes was unrelated to threshold levels measured before 16 minutes dark time. Large observational errors early in adaptation would tend to obscure an actual correlation between late and early thresholds. Early thresholds are not a good index of results which would be obtained after 25 minutes dark time.

References

1. Blanchard, Evelyn Lyman and Harper, Harold A.: Measurement of Vitamin A Status of Young Adults by the Dark Adaptation Technic. *Archives of Internal Medicine,* September, 1940, 66, pp. 661-669.

2. Booher, Lela E.; Callison, Elizabeth Crofts; and Hewston, Elizabeth M.: An Experimental Determination of the Minimum Vitamin A Requirements of Normal Adults. *Journal of Nutrition,* April, 1939, 17, No. 4, pp. 317-331.

3. Crozier, W. J.: Theory of the Visual Threshold. I. Time and Intensity. *Proceedings of the National Academy of Sciences,* January, 1940, 26, No. 1, pp. 54-60.

4. Crozier, W. J.: Theory of Visual Threshold. II. On the Kinetics of Adaptation. *Proceedings of the National Academy of Sciences,* May, 1940, 26, No. 5, pp. 334-339.

5. Fisher, R. A.: Statistical Methods for Research Workers. Edinburgh, England, Oliver and Boyd, 1925.

6. Fridericia, L. S. and Holm, E.: Experimental Contribution to the Study of the Relation Between Night Blindness and Malnutrition. *American Journal of Physiology,* June, 1925, 73, pp. 63-78.

7. Haig, Charles; Hecht, Selig; and Patek, Arthur J. Jr.: Vitamin A and Rod-Cone Dark Adaptation in Cirrhosis of the Liver. *Science,* June, 1938, 87, No. 2267, pp. 534-536.

8. Hecht, Selig: Rod, Cones and the Chemical Basis of Vision. *Physiological Reviews,* April, 1937, 17, No. 2, pp. 239-290.

9. Hecht, Selig and Mandelbaum, Joseph: The Relation Between Vitamin A and Dark Adaptation. *Journal of the American Medical Association,* May, 1939, 112, pp. 1910-1916.

10. Hecht, Selig and Mandelbaum, Joseph: Dark Adaptation and Experimental Human Vitamin A Deficiency. *American Journal of Physiology,* October, 1940, 130, pp. 651-664.

11. Hecht, Selig and Shlaer, Simon: An Adaptometer for Measuring Dark Adaptation. *Journal of the Optical Society of America,* July, 1938, No. 7, pp. 269-275.

12. Hunt, Eleanor P. and Palmer, Carroll E.: Medical Evaluation of Nutritional Status. II. Measurement of Visual Dark Adaptation With the Adaptometer. Milbank Memorial Fund *Quarterly,* October, 1940, xviii, No. 4, pp. 403-424.

13. Isaacs, Bertha L.; Jung, Frederic T.; and Ivy, Andrew C.: Clinical Studies of Vitamin A Deficiency. Biophotometer and Adaptometer (Hecht) Studies on Normal Adults and on Persons in Whom an Attempt Was Made to Produce Vitamin A Deficiency. *Archives of Ophthalmology,* October, 1940, 24, pp. 698-721.

14. Jeans, P. C. and Zentmire, Z.: The Prevalence of Vitamin A Deficiency Among Iowa Children. *Journal of the American Medical Association,* March, 1936, 106, pp. 996-997.

15. Kohlrausch, Arnt: Untersuchungen mit farbigen Schwellenprüflichtern über den Dunkeladaptationsverlauf des normalen Auges. Pflügers *Archiv für die gesamte Physiologie des Menschen und der Tiere,* July, 1922, 196, pp. 113-117.

16. Lindquist, Torsten: STUDIEN ÜBER DAS VITAMIN A BEIM MENSCHEN. Uppsala, 1938, p. 262.

17. Mack, Pauline Beery and Sanders, Agnes Pauline: The Vitamin A Status of Families in Widely Different Economic Levels. *American Journal of the Medical Sciences,* May, 1940, 199, No. 5, pp. 686-697.

18. McFarland, Ross A.: The Internal Environment and Behavior. Part I: Introduction and the Role of Oxygen. *American Journal of Psychiatry,* January, 1941, 97, No. 4, pp. 858-877.

19. McFarland, R. A. and Forbes, W. H.: The Effects of Variations in the Concentration of Oxygen and of Glucose on Dark Adaptation. *Journal of General Physiology,* September, 1940, 24, No. 1, pp. 69-98.

20. Maitra, M. K. and Harris, L. J.: Vitamin A Deficiency Among School Children in London and Cambridge. *The Lancet,* October, 1937, 2, Part 17, pp. 1009-1014.

21. Moore, L. A. and Sykes, J. F.: Cerebrospinal Fluid Pressure and Vitamin A Deficiency. *American Journal of Physiology,* October, 1940, 130, No. 4, pp. 684-689.

22. Mutch, J. R. and Griffith, H. D.: A Study of Diet in Relation to Health. Dark Adaptation as an Index of Adequate Vitamin A Intake. Technique and Preliminary Results. *British Medical Journal,* September, 1937, 2, pp. 565-570.

23. National Research Council: Chart of Recommended Daily Allowances for Specific Nutrients. Report of the Committee on Foods and Nutrition. May, 1941, Washington, D. C.

24. Pett, L. B.: Vitamin A Deficiency: Its Prevalence and Importance, as Shown by a New Test. *Journal of Laboratory and Clinical Medicine,* 1939, 25, Part 2, pp. 149-160.

25. Richards, M. B. and Irving, J. T.: Early Lesion of Vitamin A Deficiency. *Journal of Physiology,* December, 1938, 94, pp. 307-321.

26. Schultze, Max: Zur Anatomie und Physiologie der Retina. *Archiv für mikroskopische Anatomie,* April, 1866, 2, pp. 175-286.

27. Snedecor, George W.: ANALYSIS OF VARIANCE. Ames, Iowa, Collegiate Press, Inc., 1934.

28. Steffens, L. F.; Bair, H. L.; and Sheard, Charles: Photometric Measurements on Visual Adaptation in Normal Adults on Diets Deficient in Vitamin A. *Proceedings of the Staff Meetings of the Mayo Clinic,* November, 1939, 14, No. 44, pp. 698-704.

29. Stewart, C. P.: Experiments with the Dark Adaptation Test. *Journal of Physiology,* Proceedings of the Physiological Society, June, 1939, 96, pp. 28-29.

30. Tansley, K.: The Regeneration of Visual Purple. Its Relation to Dark Adaptation and Night-Blindness. *Journal of Physiology,* April, 1931, 71, Part 4, pp. 442-458.

31. Wald, George; Jeghers, Harold; and Arminio, Joseph: An Experiment in Human Dietary Night-Blindness. *American Journal of Physiology,* September, 1938, 123, No. 3, pp. 732-746.

HEMOGLOBIN VALUES IN PENNSYLVANIA MASS STUDIES IN HUMAN NUTRITION[1]

PAULINE BEERY MACK, PH.D.; JANICE MINERVA SMITH, PH.D.; CATHERINE H. LOGAN; AND ANNE THERESA O'BRIEN[2]

IN COOPERATION WITH

JOHN J. SHAW, M.D.[3]; AND PAUL DODDS, M.D.[4]

THE appraisal of the status of nutrition in human beings is commanding widespread notice at the present time because of the recognition of the need for valid techniques for this purpose, if bad dietary practices are to be altered favorably. At present, no single measure of nutritional status as a whole is regarded as being adequate, nor is evidence at hand that a satisfactory one-test technique may be developed in the near future. For those whose resources are limited, however, the number of nutritional tests used must be small, and the tests must be selected on the basis of the information which they will yield.

In connection with the mass studies in human nutrition carried on at The Pennsylvania State College since 1935, in which the Department of Health of the Commonwealth of Pennsylvania has cooperated since 1936, the test for hemoglobin has yielded results of sufficient interest to commend it for consideration by those seeking to appraise nutritional status in human beings, whether the number of tests used is extensive or limited. With the isolation of hemoglobin in crystalline form by Funk (8) in 1851, and the development of a clinical method for hemoglobin estimation by Welcher (33) in 1854—probably the first method of this sort proposed—an

[1] Authorized for publication on October 16, 1940, as Paper Number 994 in the Journal Series of the Pennsylvania Agricultural Experiment Station. Authorized on October 5, 1940, as Paper Number 8 in the Human Nutrition Research Series, published by staff members of the Ellen H. Richards Institute, The Pennsylvania State College.

[2] From The Pennsylvania State College.

[3] Secretary of Health, Commonwealth of Pennsylvania. (Deceased June 24, 1941.)

[4] Director of the Division of Maternal and Child Health, Commonwealth of Pennsylvania.

impressive succession of reports has appeared on hemoglobin methodology, and on the findings on human beings obtained by means of the hemoglobin tests developed.

Subjects of the Study

In the Pennsylvania mass studies in human nutrition carried on during the past five years, hemoglobin values have been obtained on 2,400 subjects in the following groups: 100 urban families, including 418 persons—205 males and 213 females—taken from the work of Agnes Pauline Sanders (30); 100 rural families, including 490 persons—246 males and 244 females; and 1,492 children in addition to those in the families previously mentioned—691 males and 801 females, in four different communities.

The urban families were selected in towns and small cities of sub-metropolitan size, to represent a wide range of annual cash income. The rural families were chosen in Adams, Centre, and Lancaster Counties, on the basis: (a) of the type of farm enterprise; and (b) of farm cash receipts. In Adams County (Locality 1), apple production was the chief, and frequently sole enterprise; in Centre County (Locality 2) general farming was carried on, but the level of cash farm incomes was not high; in Lancaster County (Locality 3) dairy farming was coupled with general farming, and the cash farm incomes were higher than in Locality 2. In each of the farm localities, families were selected so as to represent the distribution of annual cash farm incomes characteristic of the locality.

The school children included in this study were from the intermediate grades of public and private schools of four communities, and were selected from families for which the income distributions were typical of the respective communities as a whole. Community 1 was a city of about 82,000 inhabitants, in which railroad shops operating on a much reduced scale for many years were the leading industry. Community 2 was a college town of about 7,000 inhabitants. Community 3 was a rural community in the apple region of

southern Pennsylvania, where the children studied were in one consolidated and in two one-room schools. Community 4 was a city which, with its suburbs, had a population of about 125,000, located in the Pennsylvania anthracite region. The number of children of foreign-born parents or grandparents was higher in Community 4 than in any of the other communities. The number of children tested in the respective communities were:

Community 1	428 children —	166 boys, and	262 girls;
Community 2	147 children —	70 boys, and	77 girls;
Community 3	104 children —	59 boys, and	45 girls;
Community 4	813 children —	396 boys, and	417 girls.

No subjects were included in the study who were known to have a chronic or temporary illness which might interfere with the nutrition tests. In the family study, advice of family physicians was taken on this point. In Community 1 of the child nutrition study, each child was given an examination by the school physician, and in Communities 2, 3, and 4 by a pediatrician associated with the study, in order to exclude those whose responses to the nutrition tests might be affected by conditions other than dietary intake.

Hemoglobin Method

The standard Newcomer method was used to determine the amount of hemoglobin in the blood in terms of grams of hemoglobin per 100 cc. of blood. By this method, two samples, each of 0.01 cc. of blood were drawn into a hemoglobin micro-pipette from a single prick made in the finger by a spring lancet. Each sample was diluted to 5 cc. with 0.1 N hydrochloric acid in a special micro-pipette, and the mixture was discharged into dry Pyrex tubes, where it was allowed to stand for at least 25 minutes. At the end of this time treated samples were matched against a standard Newcomer plate in a colorimeter of the Duboscq type, and the grams of hemoglobin per 100 cc. of blood were calculated from the readings. The average of the results from the two samples was taken.

Results of the Study

Distribution of Individual Cases. The distribution of hemoglobin values according to age of all male and female subjects in the urban family part of the study, is shown in Figure 1. The same distribution for the subjects in the rural family part of the study is given in Figure 2. These case distribution diagrams show a wider range of hemoglobin values for the urban than for the rural subjects, in both sexes and throughout the age groups. There was no marked tendency for the values for either urban or rural subjects to concentrate around a central part of the range.

The dietaries of the urban and rural families will not be discussed until a later paper, except to say that the rural diets showed far less variety in type than did those of the urban families.

Although the hemoglobin values are scattered in the two units of the family study for subjects of the same sex and age, particularly in the case of the urban subjects, a tendency is seen for a lower number of grams of hemoglobin per 100 cc. of blood to be found in young children of both sexes than in older subjects, and for a higher value to be associated with males above 12 years of age than with females of the same age range.

The average hemoglobin values for the various units of the study are given in Table 1 by sex and the following age groups: from birth up to the fourth birthday, from the fourth birthday to the sixth, from the sixth birthday to the twelfth, from the twelfth to the seventeenth, from the seventeenth to the twentieth, from the twentieth to the fortieth, and from the fortieth birthday up. Values for all of the children in the study from 6 to 19 years of age were further averaged by one-year intervals for each of the sexes separately, with the averages given in Table 2.

Average Hemoglobin Values. A diagram showing the average hemoglobin values, by sex and age groups, of all of the 2,400 subjects in the study, is shown in Figure 3. In this diagram the children are

Fig. 1. Distribution of hemoglobin values of males (left) and of females (right) by individual cases, according to age, in urban-family group.

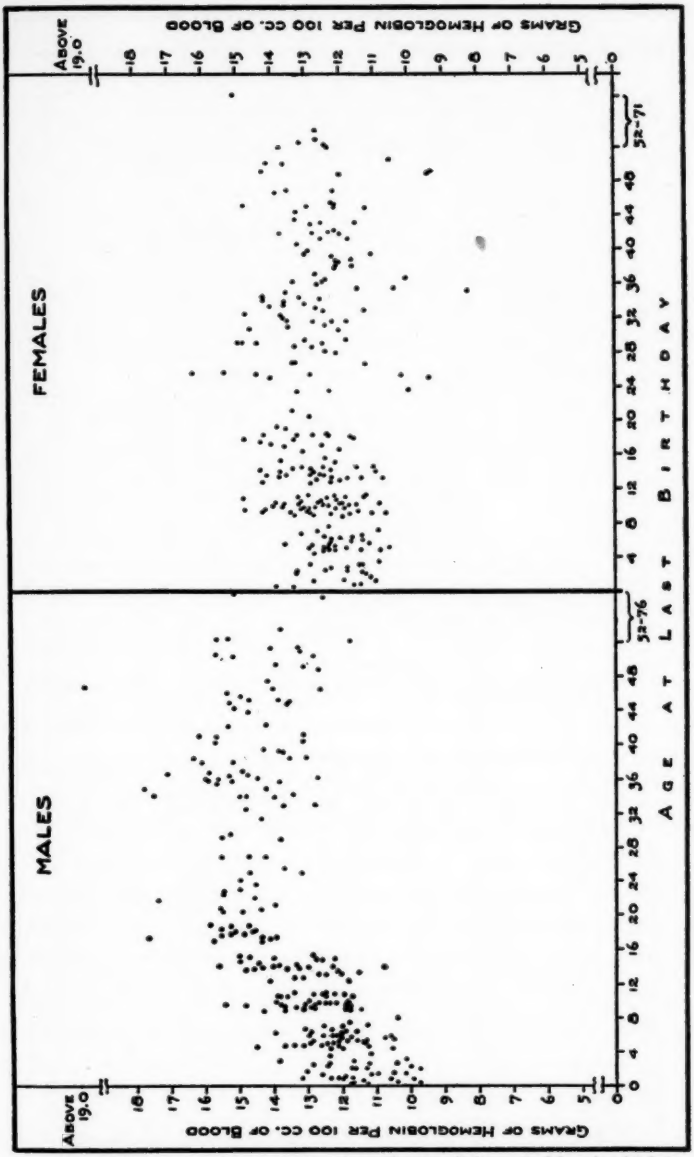

Fig. 2. Distribution of hemoglobin values of males (left) and of females (right) by individual cases, according to age, in rural-family group.

Age Range (Years)	Average Grams of Hemoglobin per 100 cc. Blood							
	Urban Families		Rural Families		School Children		All Subjects	
	Males	Females	Males	Females	Males	Females	Males	Females
Birth to 4 Years	9.72	11.22	11.40	11.18	x	x	10.61	11.16
4 to 5	11.16	10.70	12.05	12.07	11.66	11.12	11.62	11.27
6 to 11	11.29	11.61	12.59	12.59	12.92	12.63	12.79	12.59
12 to 16	14.49	13.88	13.87	13.12	12.93	12.29	13.29	12.68
17 to 19	15.57	14.13	14.97	13.26	15.18	13.24	15.16	13.57
20 to 39	12.22	12.11	14.88	12.75	x	x	13.80	12.40
40 and Above	13.09	12.18	14.35	12.58	x	x	13.62	12.40
	Number of Persons							
Birth to 4 Years	31	26	36	20	x	x	67	46
4 to 5	21	18	19	16	33	28	73	62
6 to 11	42	24	57	58	535	648	634	730
12 to 16	16	24	36	36	120	122	172	182
17 to 19	5	9	10	10	3	3	18	22
20 to 39	51	72	53	67	x	x	104	139
40 and Above	39	40	35	37	x	x	74	77

Table 1. Average hemoglobin values for males and females in different units of the study, by age groups.

Table 2. Average hemoglobin values for all males and females in the study from 6 to 20 years, by year of age.

Age at Last Birthday	Average Grams of Hemoglobin per 100 cc. of Blood		Number of Children	
	Males	Females	Males	Females
6 Years	12.07	11.34	32	17
7	11.99	11.60	39	32
8	11.98	12.00	48	73
9	12.85	12.37	86	121
10	12.93	13.00	264	314
11	12.98	12.56	165	173
12	12.99	12.37	75	86
13	13.06	13.12	43	36
14	13.19	12.51	28	24
15	14.24	13.06	9	18
16	14.80	13.10	17	18
17	16.63	13.97	7	8
18	14.50	12.92	5	8
19	13.99	13.90	6	6

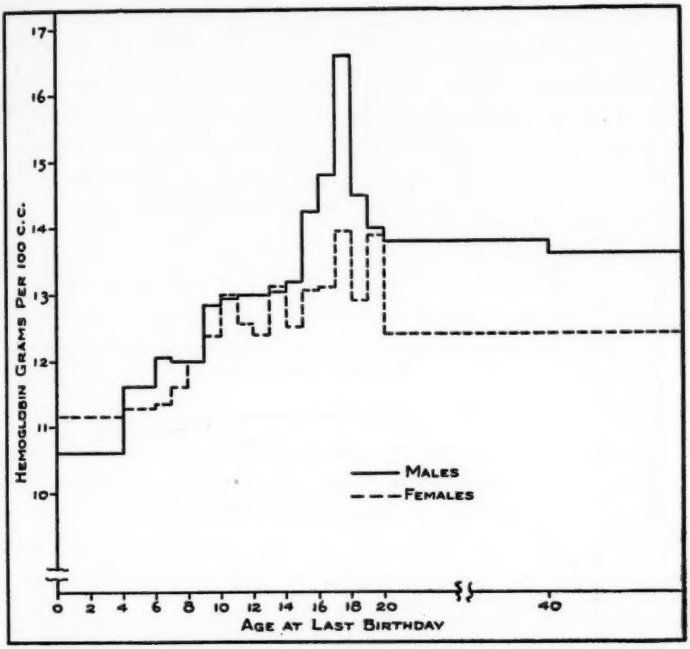

Fig. 3. Average hemoglobin values of all male and female subjects in the study according to age.

shown by one-year intervals from the sixth to the twentieth birthday. Although the sexes were not found to be significantly different in hemoglobin values below 12 years of age, the average values for age groups of each sex under 6 years of age were significantly lower than those for every other age group. Males were found to be significantly higher than females for all age groups beyond 12 years. Both sexes showed marked increases during the ages when puberty is most likely to occur, after which values decreased sharply and remained at a constant average for age groups 20 to 40 years and 40 years and older.

The average number of grams of hemoglobin per 100 cc. of blood for the subjects in the urban family part of the study, by age groups,

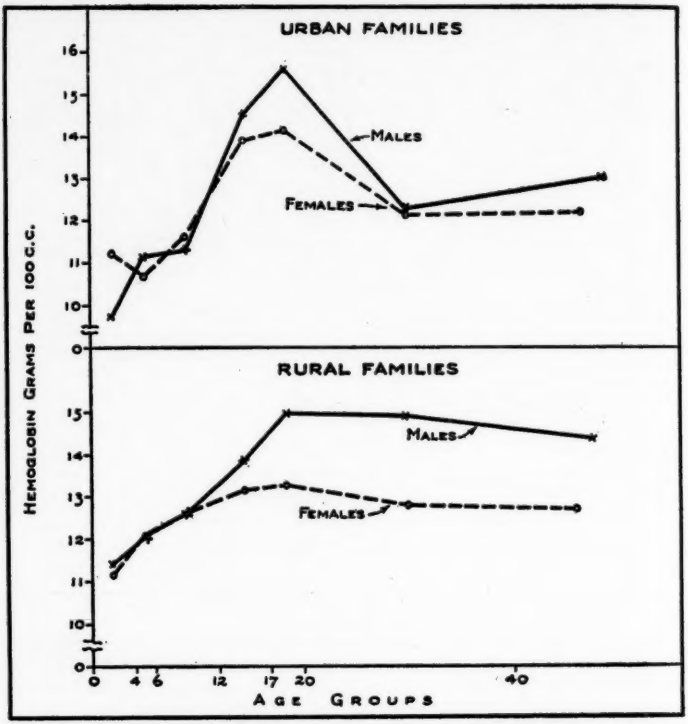

Fig. 4. Average hemoglobin values according to age for males and females in the urban-family group (upper section) and in the rural-family group (lower section).

is given in the upper section of Figure 4, with the sexes graphed separately. The chief distinction between the average urban hemoglobin values shown in this graph and those for all of the subjects of the study, given in Figure 3 previously cited, lies in the fact that a much greater average difference was found between the children up to 12 years of age and all other age groups than was present among the averages for all of the subjects combined, and in the further fact that the urban males over 20 years of age were lower than rural males of the same age group.

The average hemoglobin values of all male and female subjects in the rural family part of the study are graphed according to age in the lower section of Figure 4. The hemoglobin value differences between the younger children and the other subjects in the group were not so extreme as were those of the urban group. Instead, a gradual, but slight, increase in grams of hemoglobin per 100 cc. of blood was found from one age group to the next, for both sexes, up to the 12-to-17 year group. There was but little decrease, however, after 40 years. The average values for rural males in the older age groups were greater than for the corresponding ages in the urban group, as has been mentioned, although the same was not true for females.

Percentage Distribution According to Hemoglobin Values. In order to make comparisons among certain groups in the study as to the percentage of subjects found within certain ranges of hemoglobin values, five arbitrary ranges of response to the hemoglobin test were established as follows: (1) 13.0 or more grams of hemoglobin per 100 cc. of blood; (2) from 11.5 to 12.99 grams; (3) from 10 to 11.49 grams; (4) from 7.5 to 9.99 grams; and (5) below 7.5 grams.

The percentages of all males and of all females in the study, by age groups, within each of the defined ranges of hemoglobin values are shown in Figure 5. The same broad differences between the younger children and all other age groups, and between the sexes after 12 years of age are apparent in these distribution graphs. For example, the percentage both of males and of females in the higher hemoglobin ranges tends to increase while that in the lower ranges decreases as the ages become greater up to the 17-to-20 year group. A higher number of males than of females was found in the higher hemoglobin ranges after 12 years of age.

The percentages of all of the subjects in the urban families and that of the children in these families who were of grade school age (from 6 to 15 years old) in the different ranges of hemoglobin

MALES
FEMALES
PERCENTAGE OF SUBJECTS
GRAMS OF HEMOGLOBIN PER 100 c.c. BLOOD
FROM BIRTH TO 6 YRS.
FROM 6½ TO 12 YEARS
FROM 12½ TO 17 YEARS
FROM 17½ TO 20 YEARS
FROM 21+ TO 40 YEARS
40 YEARS AND ABOVE
FROM BIRTH TO 6 YEARS
FROM 6½ TO 12 YEARS
FROM 12½ TO 17 YEARS
FROM 17 TO 20 YEARS
FROM 20 TO 40 YEARS
40 YEARS AND ABOVE

Fig. 5. Percentage distributions of males and of females in specific age groups according to hemoglobin values; all subjects in family unit studies and in school groups are included.

values, are given in Figure 6. The respective percentages for the rural families are likewise shown in the same figure. The higher percentage of all persons, and also of children of grade school age, in the rural families in the higher hemoglobin ranges as compared with that of persons in the urban families, is strikingly apparent.

For the rural families grouped according to type of farm enterprise, the percentages of all subjects and of children from 6 to 15 years of age in the different hemoglobin ranges are shown in Figure 7. The three sub-groups thus formed were all somewhat superior to the urban group in the percentage of subjects in the higher hemoglobin ranges; Locality 3, representing the most prosperous general farming group, was found to be the best in this respect.

The percentages of the 1,492 children in the child nutrition study found in the different hemoglobin ranges are graphed in Figure 8; the different community groups are shown separately. Community 1, previously reported by Zayaz, Mack, Sprague, and Bauman (39), representing a small industrial city of long-time economic depression, was the lowest in the percentage of children in the higher hemoglobin classes. This community, for example, had but 1.2 per cent of the children in the sample in the highest arbitrary hemoglobin range, with but 41.2 per cent in the next highest. The other three communities had 96.5, 97.2, and 97.4 per cent of the children in the highest two ranges. Community 2 (a small college town) had a slightly smaller percentage in the highest hemoglobin range than did Community 3 (a rural community), or Community 4 (another industrial community in better economic circumstances than Community 1). In Community 4, there was a larger percentage of children of foreign-born parents or grandparents than in any of the other three communities (in all of which there was only a small proportion of children of foreign extraction). In this community, the eating habits of the children tended to be different from those of similar income families in the other communities, a fact which is believed to be associated with their better hemoglobin status. As

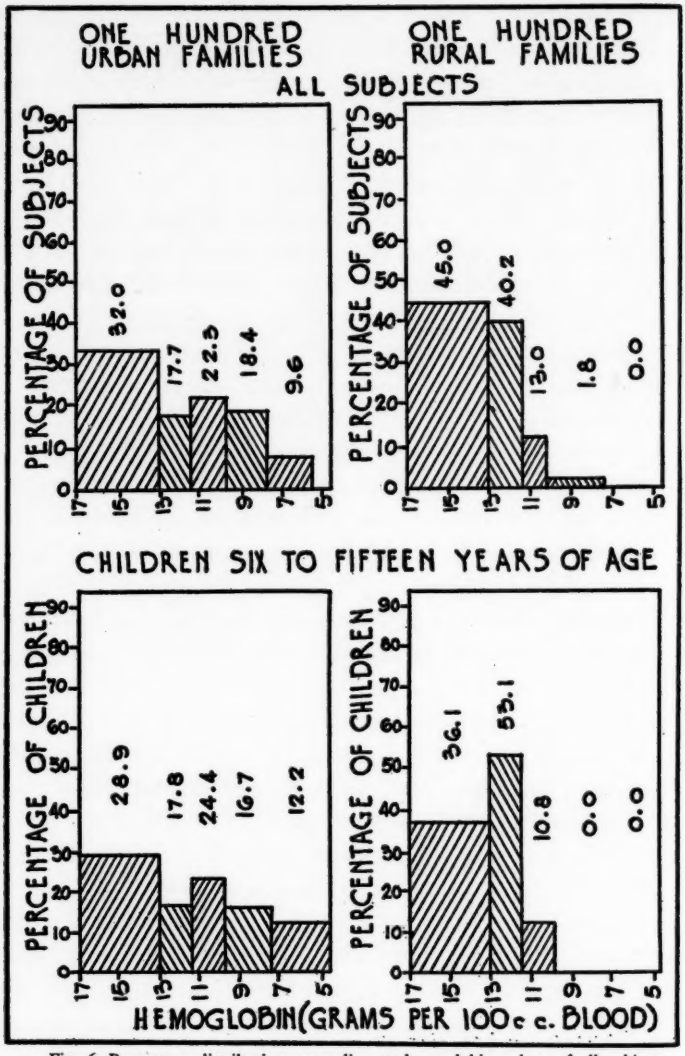

Fig. 6. Percentage distributions according to hemoglobin values of all subjects and of children six to fifteen years of age in the urban-family group and in the rural-family group.

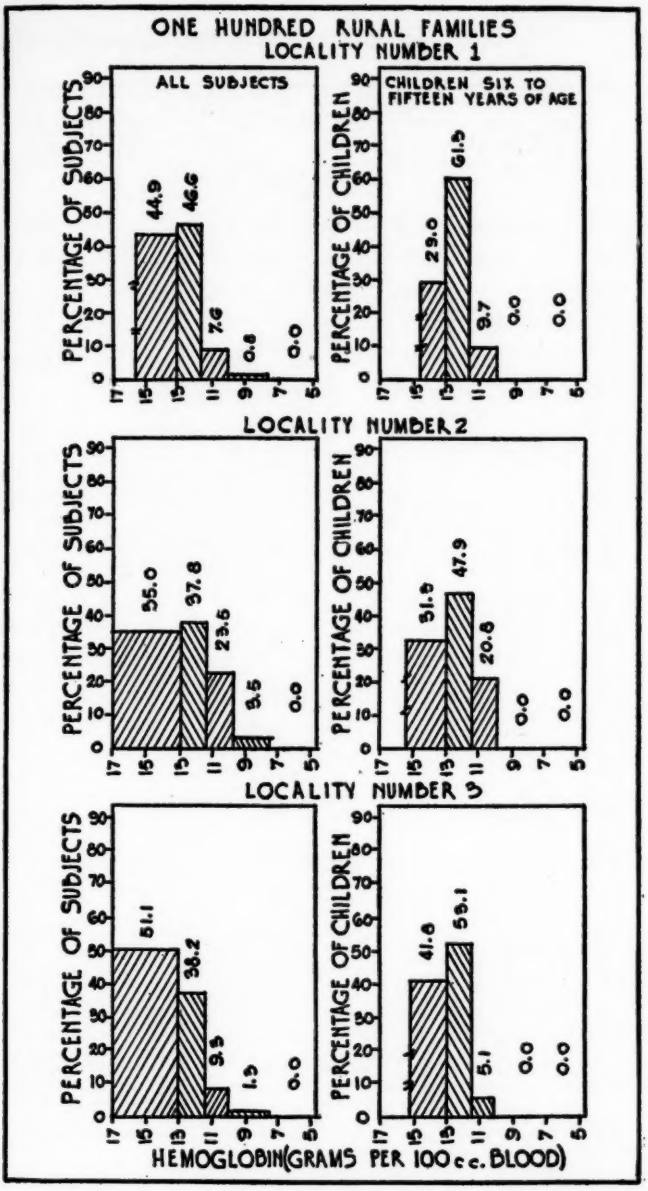

Fig. 7. Percentage distributions according to hemoglobin values of all subjects and of children six to fifteen years of age in each of three localities included in the rural-family group.

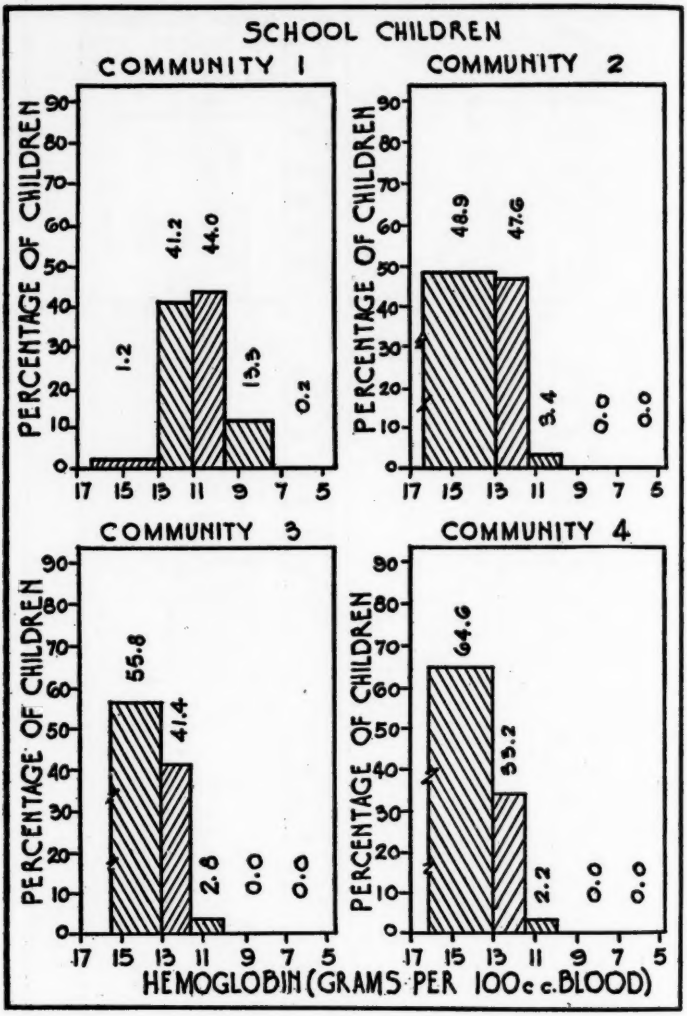

Fig. 8. Percentage distributions according to hemoglobin values of grade-school children in each of four communities.

has been mentioned, the diets of the subjects in this study in relation to hemoglobin status will be discussed in a later report.

Comparison with Other Investigations

In comparing the results of the Pennsylvania hemoglobin measurements with those of other investigators, Mugrage and Andresen (19) in a study of 200 children from birth to 3 years of age state that infants have high hemoglobin values at birth, which decrease in infancy to a minimum at the third or fourth month, with no appreciable increase during the first two years. This substantiates earlier findings by Appleton (2), Drucker (4), Elvehjem, Peterson, and Mendenhall (5), MacKay (15), Merritt and Davidson (16), and Williamson (35). Although there were no new-born infants in the present study, the findings with respect to infants and young children are in conformity with those of the investigators just cited. As has been pointed out, children in this study below 6 years of age had significantly lower hemoglobin values than the subjects in all other age groups, although no sex differences which were statistically significant were found below 12 years of age.

It is generally agreed that there is no sex difference in hemoglobin up to 12 to 13 years of age, in conformity with the results of this study. Mugrage and Andresen (18), for example, in a study of 533 children from birth to 13 years of age found no significant differences between average hemoglobin concentrations of boys and of girls. Similar results were reported by Osgood and Baker (24) in a survey of 215 children from 4 to 13 years of age. In a survey of 259 males and 152 females 14 to 30 years of age, Osgood (23) reported that the adult hemoglobin value for males was attained at 16 years, whereas that for girls was two years earlier. Similar results were reported by Mugrage and Andresen (19) in a study of 160 subjects 13 to 21 years of age.

Many studies have been based on the hemoglobin concentrations of the blood of supposedly normal adult male populations. Aver-

ages have been based on as few as ten cases, with a maximum of 325 cases in one report. Values ranging from 14.07 grams to 17.00 grams per 100 cc. of blood have been reported by the following investigators:

Investigators	*Locality*	*Number of Cases of Males*	*Age Range (Years)*	*Hemoglobin (Grams/100 cc.)*
Everett (6)	Pennsylvania	100	18-24	14.96
Foster and Johnson (7)	New Orleans	115	18-30	15.63
Parodi (26)	Buenos Aires	50	18-30	15.40
Wintrobe (38)	New Orleans	86	18-30	16.00
Haden (10)	Kansas City	70	18-50	15.34
Nelson and Stoker (21)	Kansas	325	18-65	14.38
Horneffer (12)	Germany	40	19-29	16.00
Haden (9)	Kansas City	40	18-50	15.50
Meyers and Eddy (17)	Cleveland	111	19-30	15.83
Osgood (22)	Oregon	137	19-30	15.76
Tien, Chia yu (31)	Manchuria	320	19-64	16.75
Sachs, Levine, and Fabian (28)	Omaha	200	20-25	14.96
Walters (32)	Kansas	100	20-30	15.12
Wintrobe (36)	New Orleans	100	20-30	17.00
Helmer and Emerson (11)	Indianapolis	18	20-40	15.66
Komacki (14)	Warsaw	17	20-40	14.79
Murphy, Lynch, and Howard (20)	Boston	18	20-40	15.06
Andresen and Mugrage (1)	Denver	40	20-45	16.87
Price-Jones (27)	London	100	20-51	14.50
Broun and Briggs (3)	St. Louis	23	Adults (age not given)	16.60
Jenkins and Don (13)	London	118	Adults (age not given)	15.85

Many of these same investigators have reported hemoglobin averages for supposedly normal adult females. These averages, together with those published by other investigators, have been uniformly lower than those listed for males. Thus, values ranging from 12.80 to 15.28 grams per 100 cc. have been given by the following:

Investigators	*Locality*	*Number of Cases of Females*	*Age Range (Years)*	*Hemoglobin (Grams/100 cc.)*
Wintrobe (38)	New Orleans	101	18-30	14.10
Everett (6)	Pennsylvania	84	18-32	13.16
Haden (10)	Kansas City	30	18-50	13.37
Widdowson and McCance (34)	England	63	18-90	12.80
Haden (9)	Kansas City	12	19-30	13.30
Osgood and Haskins (25)	Oregon	100	18-30	13.70
Sachs, Levine, and Fabian (28)	Omaha	100	20-25	12.96
Meyers and Eddy (17)	Cleveland	48	20-30	13.10
Wintrobe (37)	New Orleans	50	17-30	13.76
Helmer and Emerson (11)	Indianapolis	10	20-40	13.68
Murphy, Lynch, and Howard (20)	Boston	21	20-40	13.90
Andresen and Mugrage (1)	Denver	40	20-45	14.33
Price-Jones (27)	London	100	20-51	13.60
Sackett (29)	Kansas City	——	——	15.28
Jenkins and Don (13)	London	118	Adults (age not given)	15.85
Broun and Briggs (3)	St. Louis	23	Adults (age not given)	16.60

No standards for hemoglobin are generally accepted at the present time, and there are indications that the age and sex differences

found in this study, which confirm the results of previous investigators, may be the result of dietary as well as physiological differences. Thus numerous investigators have raised the hemoglobin values of groups of preschool children and of females above the age of puberty by alterations in the diet. This may therefore lead ultimately to the adoption of standards quite different from the sex and age averages now available.

Summary

This is a report of the hemoglobin values obtained for 2,400 subjects in a mass study in human nutrition carried on in Pennsylvania from 1935 until 1940. One hundred urban families composed of 418 persons, and one hundred rural families with 490 family members were studied, in addition to 1,492 school children in four typical communities. Results have been given by age and sex, and differences in the hemoglobin values of persons in the various communities have been discussed.

Even in the absence of standards, those seeking to appraise the status of nutrition at the present time can well consider hemoglobin determinations as valuable, in view of the wide distribution of values found in the subjects of this study. Thus, rural subjects have been found to be more nearly uniform in value than urban, although even in the former group, women of childbearing age average lower than is certainly desirable. Children of preschool age in the urban families are much lower than those in the same age groups among the rural families, and it may be assumed that their average status is poorer in this respect since there is no occasion to doubt that increased hemoglobin values are generally associated with improved nutritional status, within any age group. Children in an economically depressed industrial community were found to be exceptionally low in hemoglobin values, as compared with those in other communities in better economic condition; scattered cases in all sex and age groups in all parts of the study were far below the

average of the group. These results indicate that, on an individual case basis, instances of poor nutritional status with respect to hemoglobin may be found, even if the optimum status with respect to this value has not yet been ascertained for various ages of the two sexes.

References

1. Andresen, M. I. and Mugrage, E. R.: Red Blood Cell Values for Normal Men and Women. *Archives of Internal Medicine*, 1936, 58, p. 136.

2. Appleton, V. B.: Determination of Hemoglobin During Infancy by the Palmer and Van Slyke Methods. *Journal of Biological Chemistry*, 1918, 34, p. 369.

3. Broun, G. O. and Briggs, A. P.: Hemoglobin and Blood Count Relations as Determined by Iron and Oxygen Capacity Methods. *Journal of Laboratory and Clinical Medicine*, 1934, 19, p. 886.

4. Drucker, P.: Investigations on the Normal Values for the Hemoglobin and Cell Volume in the Small Child. *Acta Paediatrica*, 1923, 3, p. 1.

5. Elvehjem, C. A.; Peterson, W. N.; and Mendenhall, D. K.: Hemoglobin Content of the Blood of Infants. *American Journal of Diseases of Children*, 1933, 46, p. 105.

6. Everett, Ruth: A Study of the Erythrocyte Counts and Hemoglobin Values for Normal College Men and Women. (M. S. Thesis). The Pennsylvania State College, 1937.

7. Foster, P. C. and Johnson, J. R.: Oxygen Capacity and Hemoglobin Content of Normal Blood of Men. *Proceedings of the Society for Experimental Biology and Medicine*, 1930-1931, 28, p. 929.

8. Funk, O.: Ueber das Milzyvenenblut. *Zeitschrift für rat. Medizin, N. S.* 1851, 31, p. 172.

9. Haden, R. L.: Accurate Criteria for Differentiating Anemias. *Archives of Internal Medicine*, 1923, 31, p. 766.

10. Haden, R. L.: Hemoglobin Standards. *American Journal of Clinical Pathology*, 1933, 3, p. 85.

11. Helmer, O. M. and Emerson, C. P.: Iron Content of Whole Blood of Normal Individuals. *Journal of Biological Chemistry*, 1934, 104, p. 157.

12. Horneffer, L.: Das Blut des Menschen, mit neuren Methoden Untersucht. *Pflügers Archiv für die gesamte Physiologie des Menschen und der Tiere*, 1928, 220, p. 703.

13. Jenkins, C. E. and Don, C. S. D.: The Hemoglobin Concentration of Normal English Males and Females. *Journal of Hygiene*, 1933, 33, p. 36.

14. Komacki, W.: Uber die Zahl der roten Blut körperchen bei gesunden erwachsenen Menschen. *Virchow's Archiv für pathologische Anatomie und Physiologie und für klinische Medizin*, 1924, 253, p. 386.

15. MacKay, H. M. M.: Normal Hemoglobin Level during First Year of Life. *Archives of Disease in Childhood*, 1933, 8, p. 221.

16. Merritt, K. K. and Davidson, L. T.: The Blood during the First Year of Life. *American Journal of Diseases of Children*, 1933, 46, p. 990.

17. Meyers, V. C. and Eddy, H. M.: The Hemoglobin Content of Human Blood. *Journal of Laboratory and Clinical Medicine*, 1939, 24, p. 502.

18. Mugrage, E. R. and Andresen, M. I.: Values for Red Blood Cells of Average Infants and Children. *American Journal of Diseases of Children*, 1936, 51, p. 775.

19. Mugrage, E. R. and Andresen, M. I.: Red Blood Cell Values in Adolescence. *American Journal of Diseases of Children*, 1938, 56, p. 997.

20. Murphy, W. P.; Lynch, R.; and Howard, I. M.: The Value of Determinations of the Iron Content of Whole Blood. *Archives of Internal Medicine*, 1931, 47, p. 883.

21. Nelson, C. F. and Stoker, R.: The Hemoglobin Concentration and Red Blood Cell Count of Healthy Men. *Journal of Biological Chemistry*, 1936, 114, lxxvi.

22. Osgood, E. E.: Hemoglobin, Color Saturation Index and Volume Index Standards. *Archives of Internal Medicine*, 1926, 37, p. 685.

23. Osgood, E. E.: Normal Hematologic Standards. *Archives of Internal Medicine*, 1935, 56, p. 849.

24. Osgood, E. E. and Baker, R. L.: Erythrocyte, Hemoglobin, Cell Volume and Color, Volume and Saturation Index Standards for Normal Children of School Age. *American Journal of Diseases of Children*, 1935, 50, p. 343.

25. Osgood, E. E. and Haskins, H. D.: Relation Between Cell Count, Cell Volume and Hemoglobin Content of Venous Blood of Normal Young Women. *Archives of Internal Medicine*, 1927, 39, p. 643.

26. Parodi, A. S.: Numero de Eritrocitos v Volumen Globular Humanos en Buenos Aires. *Revista de la Sociedad argentina de biologia y sus filiales la Sociedad de biologia de Rosario y la Sociedad de Biologia de Córdoba*, 1930, 6, p. 426.

27. Price-Jones, C.: The Concentration of Hemoglobin in Normal Human Blood. *Journal of Pathology and Bacteriology*, 1931, 34, p. 779.

28. Sachs, A.; Levine, V. E.; and Fabian, A. A.: Copper and Iron in Human Blood. *Archives of Internal Medicine*, 1935, 55, p. 227.

29. Sackett, G. E.: Hemoglobin and Iron in Blood. *Journal of Laboratory and Clinical Medicine*, 1924-1925, 10, p. 1018.

30. Sanders, Agnes Pauline: The Dietary Habits and Nutritional Status of 100 Pennsylvania Urban Families. (Ph.D. Dissertation). The Pennsylvania State College, 1937.

31. Tien, Chia yu: On the Normal Blood Picture of Chinese. *The Journal of Oriental Medicine*, 1931, 14, p. 40.

32. Walters, O. S.: Normal Erythrocyte, Hemoglobin and Packed Cell Volume Standards in Young Men. *Journal of Laboratory and Clinical Medicine*, 1933-1934, 19, p. 851.

33. Welcher, H.: Blutkörperchen Zahlungen und farbenprüfende Methoden. *Vierteljahrschrift für die praktische Heilkunde u.s.*, 1854, 11, p. 11.

34. Widdowson, E. M. and McCance, R. A.: Iron in Human Nutrition. *Journal of Hygiene*, 1936, 36, pp. 13-24.

35. Williamson, C. S.: Influence of Age and Sex on Hemoglobin. *Archives of Internal Medicine*, 1916, 18, p. 505.

36. Wintrobe, M. M.: Hemoglobin Standards in Normal Men. *Proceedings of the Society for Experimental Biology and Medicine*, 1928-1929, 26, p. 848.

37. Wintrobe, M. M.: Blood of Normal Young Women Residing in a Subtropical Climate. *Archives of Internal Medicine*, 1930, 45, p. 287.

38. Wintrobe, M. M.: Blood of Normal Men and Women, Erythrocyte Counts, Hemoglobin and Volume of Packed Red Cells of 229 Individuals. *Bulletin of the Johns Hopkins Hospital*, 1933, 53, p. 118.

39. Zayaz, Stella Louise; Mack, Pauline Beery; Sprague, Phyllis Kent; and Bauman, Arthur W.: Nutritional Status of School Children in a Small Industrial City. *Child Development*, March, 1940, 2, No. 1, p. 1.

CONTRACEPTIVE SERVICE IN THREE AREAS

PART II. THE EFFECTIVENESS OF CLINIC SERVICES

REGINE K. STIX, M.D.[1]

INTRODUCTION

MOST birth control services in the United States have fairly uniform policies, regardless of the types of women they serve or the environment from which their patients come. The diaphragm and jelly or some variation of that technique, which involves the combination of a spermicide and an occlusive covering for the cervix, have been almost universally considered the only methods suitable for prescription. In rural areas, where there are no clinics, the choice has been jelly alone or sponge and foam powder; in clinics, where individual fitting is possible, the diaphragm or cervical cap with jelly has been prescribed for almost every patient.

The wisdom of such single-mindedness is open to question. The use of contraception is a highly personal and individual problem and it seems unlikely that a single type of contraception could be acceptable to all couples. Recently completed surveys of three clinics, in New York City; in Cincinnati, Ohio; and in Spartanburg, South Carolina, permit the study of the results of the present restricted policies for widely differing groups of patients.

The characteristics of the patients in each area and their fertility before clinic attendance have been discussed in detail in a previous article.[2] The patients of the three clinics were very different. The women who attended the Birth Control Clinical Research Bureau, in New York City, were mainly foreign-born Jewish women who had shown a special interest in controlling their fertility. Most of them came to the clinic on their own initiative and paid for the

[1] From the Milbank Memorial Fund.

[2] Stix, Regine K.: Contraceptive Service in Three Areas: Part I. The Clinics and Their Patients. The Milbank Memorial Fund *Quarterly*, April, 1941, xix, No. 2, pp. 171-188.

service given them. Almost all of them had used contraception quite effectively for most of their married life before they attended the clinic, but they came to the clinic in the hope of finding more acceptable contraceptive techniques.

In Cincinnati most of the patients were relief recipients or wives of manual workers with small incomes, who were referred for contraceptive advice by social workers or physicians because their families were large and the mothers needed to be spared the burden of additional pregnancies. Almost all of them had made some attempt to use contraception before attending the clinic but their contraceptive practice had not been very effective. Their uncontrolled fertility was lower than that of the New York women but, because they used contraception less extensively as well as less effectively, their total fertility was considerably higher.

The Spartanburg clinic is a referral service in the Spartanburg General Hospital, under the supervision of the County Health Department, which serves both white and Negro women from rural and urban sections of a southern cotton county. Its patients are sent to the clinic mainly because of illness contraindicating further pregnancy. Those referred during the period of study were the wives of urban manual workers, of sharecroppers, and of farm tenants, whose economic status was very low. Their total fertility was high because they married early and used little contraception. Their uncontrolled fertility, however, was lower than that of the women in Cincinnati or New York because of the extensive prevalence of pelvic and endocrine disease, of syphilis, and of pellagra.

The patients of the Spartanburg clinic presented a problem similar to that in Cincinnati, in that there was little use of effective contraception before clinic attendance. The problem was more complex than that in Cincinnati because a much larger proportion of couples had never used any contraception and few of the clinic patients could afford to buy commercial contraceptives. The proportions of urban couples using any contraception before attending

the clinic were significantly higher than those of farm families. Sixty-five per cent of white and 28 per cent of Negro urban couples had made some attempt to use contraception, while only 48 per cent of the white and 19 per cent of the Negro couples employed on farms had ever used any contraceptive technique. Thus, the problem of training patients to the consistent use of contraceptives was especially difficult in Spartanburg where, for most of the women, serious impairment of health made it essential that pregnancy be prevented.

The policies of all three clinics were alike in that an occlusive rubber device, usually a diaphragm, and jelly, to be used by the wife, were prescribed for 90 per cent or more of the patients in each clinic (Table 5). Cervical caps were prescribed for 15 per cent of the New York patients, but were not given to any patients in Spartanburg or in Cincinnati. The clinician in Spartanburg attempted to vary the prescription if the diaphragm was unsuitable for any specific patient, but, because in most cases the patient's health made it imperative that pregnancy be avoided or at least delayed, she was

Table 5. Types of contraception prescribed for the patients of three clinics.

Contraceptive Method Prescribed	White Patients of:			Negro Patients of Spartanburg Maternal Health Clinic
	Clinical Research Bureau (N.Y.C.)	Cincinnati Maternal Health Clinics	Spartanburg Maternal Health Clinic	
	Number of women			
	991	1,609	530	457
	Per cent for whom each method was prescribed			
Diaphragm and Jelly	79.0	98.0	89.6	92.6
Cervical Cap and Jelly	14.7	—	—	—
Condom and Jelly	1.6	—	0.8	0.2
Sponge and Jelly or Powder	2.4	—	1.3	2.6
Jelly Alone	2.2	2.0	0.2	—
Diaphragm and/or Sponge	—	—	4.9	4.4
Diaphragm and/or Condom	—	—	2.8	—
Other	—	—	0.4	0.2

unwilling to prescribe any techniques other than those she considered completely reliable.

Measuring the Effectiveness of Clinic Services

The problem of measuring the impact of clinic attendance on a group of patients is a highly complex one. The process involves not only the measurement of the effectiveness of the prescribed techniques in preventing pregnancy for those women who use them, but also of the acceptability of those techniques for the whole group of patients, since even the best contraceptive can protect only those women who use it. The measurement of acceptability includes ascertaining the proportion of patients who never used the prescribed contraceptives, who used them throughout the survey period, and who used them and then gave them up, and the analysis of the reasons for their rejection on the part of those women who never used them or who abandoned them after a period of trial.

It has been found that clinic patients use all contraception more effectively after they have attended a birth control clinic.[8] Thus, the clinic may be partly responsible for a drop in fertility postclinic, attributable to the better use of contraceptives other than those prescribed. After clinic attendance the fertility of the patients who continue to use contraception can be expected to remain low, therefore, regardless of the types of contraception used. On the other hand, if some of them should abandon the use of contraception entirely, after a period of trial of the prescribed contraceptives, group fertility would be expected first to drop and then to rise. Such a rise might not make itself evident in the brief postclinic period during which the patients are usually under observation. The data must therefore be analyzed with care and interpreted with caution.

The Effectiveness of Clinically Prescribed Contraceptives. In all

[8] Stix, Regine K. and Notestein, Frank W.: Controlled Fertility. Baltimore, The Williams and Wilkins Company, 1940, p. 110, Table 49.

Stix, Regine K.: Birth Control in a Midwestern City. Part II. The Milbank Memorial Fund *Quarterly*, April, 1939, xvii, No. 2, p. 167, Table 22.

three of the areas under consideration, the contraceptives prescribed by the clinics proved highly effective for those patients who used them. Pregnancy rates for all use of the prescribed contraceptives and rates for those periods during which they were used exclusively are shown for the three groups of white and one of Negro patients in Table 6.[4] Variants of the clinic prescription (its alternate use with other contraceptives or no contraception,[5] or the use of only part of the method) were used during part of the postclinic exposure of all groups. The proportion of exposure during which variants were used, however, was small for all clinics; and the inclusion of this experience had little effect on the rates for the clinic prescription.

All rates for the prescribed contraceptives were low, and differences between the rates for the four groups of women were small.[6] The rates of the New York women for all use of the clinic prescription were significantly lower than those for any of the other groups. For periods during which the prescribed contraceptives were used exclusively, however, no difference was highly significant. None of the rates for Negroes was different from the corresponding rate for white women in Spartanburg. Differences might have been greater had there been a larger body of experience, but it appears justifiable to conclude that even for the Negro women the diaphragm and jelly proved highly effective.

[4] The rates shown are those for pregnancies per 100 years' exposure to the risk of pregnancy for each group. The "exposure" of each woman was calculated by deducting time pregnant and all periods of separation of husband and wife from the total number of years between the initial clinic contact and the date of closing the record. Exposures of women with similar experience (as with clinic prescription) were then added and divided into the number of pregnancies occurring in the aggregate experience. The resulting rate was multiplied by 100 for convenience, in order to express it as a whole number. Rates for clinic prescription include the use of all the contraceptives prescribed.

[5] The alternate use of clinic prescription and no contraception was found rarely in New York and Cincinnati, but constituted 6 per cent of the exposure with clinic prescription of Spartanburg white women and 10 per cent of that of the Negro women. This sporadic use of contraception by the Spartanburg group could not be ignored and therefore was included as part of the group practice.

[6] The χ^2 test was used to determine the differences between rates. The test is not ideally suited to the type of data presented, but is the only one applicable. Except for differences noted in the text, all values of p for comparisons of rates shown in Table 6 fell between .03 and .09.

Table 6. Pregnancy rates with clinically prescribed contraceptives for four groups of women.

Period of Married Life	White Patients of:			Negro Patients of Spartanburg Maternal Health Clinic
	Clinical Research Bureau (N.Y.C.)	Cincinnati Maternal Health Clinics	Spartanburg Maternal Health Clinic	
ALL USE OF CLINIC PRESCRIPTION[1]				
PREGNANCIES PER 100 YEARS OF EXPOSURE				
First Pregnancies	8	4	6	—[2]
All Later Pregnancies	9	11	14	16
Years Since Marriage				
0–4	12	16	14	19
5–9	11	10	17	17
10–14	5	10	15	16
15–29	5	11	11	8
EXPOSURE IN YEARS AND NUMBER OF PREGNANCIES				
	Exp. Yrs. / No. Preg.	Exp. Yrs. / No. Preg.	Exp. Yrs. / No. Preg.	Exp. Yrs. / No. Preg.
First Pregnancies	50.8 / 4	118.6 / 5	15.6 / 1	3.0 / 0
All Later Pregnancies	887.1 / 76	2,932.9 / 326	453.0 / 64	358.9 / 56
Years Since Marriage				
0–4	179.4 / 21	460.1 / 73	76.9 / 11	94.8 / 18
5–9	307.3 / 34	1,015.1 / 104	113.0 / 19	111.1 / 19
10–14	253.1 / 13	778.8 / 74	126.0 / 19	79.7 / 13
15–29	147.3 / 8	678.9 / 75	137.1 / 15	73.3 / 6
EXCLUSIVE USE OF CLINIC PRESCRIPTION				
PREGNANCIES PER 100 YEARS OF EXPOSURE				
First Pregnancies	8	3	0	—[2]
All Later Pregnancies	9	9	12	14
Years Since Marriage				
0–4	13	12	13	15
5–9	12	9	14	15
10–14	5	8	12	17
15–29	6	8	11	8
EXPOSURE IN YEARS AND NUMBER OF PREGNANCIES				
	Exp. Yrs. / No. Preg.	Exp. Yrs. / No. Preg.	Exp. Yrs. / No. Preg.	Exp. Yrs. / No. Preg.
First Pregnancies	38.4 / 3	116.1 / 4	11.8 / 0	1.8 / 0
All Later Pregnancies	703.4 / 65	2,703.1 / 244	371.1 / 46	300.2 / 41
Years Since Marriage				
0–4	150.7 / 19	442.7 / 54	60.2 / 8	80.6 / 12
5–9	249.6 / 30	935.7 / 82	94.0 / 13	93.2 / 14
10–14	195.0 / 10	713.6 / 58	109.7 / 13	60.2 / 10
15–29	108.2 / 6	611.1 / 50	107.2 / 12	66.2 / 5

[1] Includes use of variants of the prescribed contraceptives, such as alternate use of CIB and other contraceptives, etc.
[2] Less than ten years of exposure.

All use of the prescribed contraceptives prevented between 80 and 94 per cent of the pregnancies which would have been expected if the clinic patients had used no contraception for an equal period of exposure to the risk of pregnancy (Table 7). The effectiveness ratios were lowest for the Spartanburg women and highest for the New York clinic patients. It is not surprising that the Spartanburg patients were less skillful in using the diaphragm and jelly than the average patient in New York or Cincinnati. The effectiveness with which the clinic prescription was used in Spartanburg was approximately the same as that observed for relief recipients in Cincinnati, who had similar social and economic backgrounds.[7] It is probable that women in both groups were not only handicapped by the conditions under which they lived but were also poorly equipped by education and intelligence to use a complicated contraceptive technique consistently and correctly.

The hazard of accidental pregnancy with the prescribed contraceptives was greatest immediately after the initial clinic contact, and declined, first rapidly, and then gradually until the risk was

Table 7. Per cent of effectiveness of each type of contraception as used by four groups of women after clinic attendance.[1]

Type of Contraception	White Patients of:			Negro Patients of Spartanburg Maternal Health Clinic
	Clinical Research Bureau (N.Y.C.)	Cincinnati Maternal Health Clinics	Spartanburg Maternal Health Clinic	
All Contraception	93[2]	85	81	78
All Use of Clinic Prescription	94	90	81	80
Exclusive Use	93	92	84	83
Use of Variants[3]	96	64	70	68
All Other Contraceptives	91[2]	72	81	55

[1] Ratio of pregnancies prevented to those expected had no contraception been used.
[2] These ratios are slightly higher than those shown in Stix and Notestein, Table 49, because those in Table 49 were standardized to the period-of-married-life distribution of all exposures with contraception postclinic, and those presented here were not so standardized.
[3] Alternate use of CIB and other contraceptives or no contraception, or use of only part of the CIB.

[7] Stix, 1939, p. 167, Table 22.

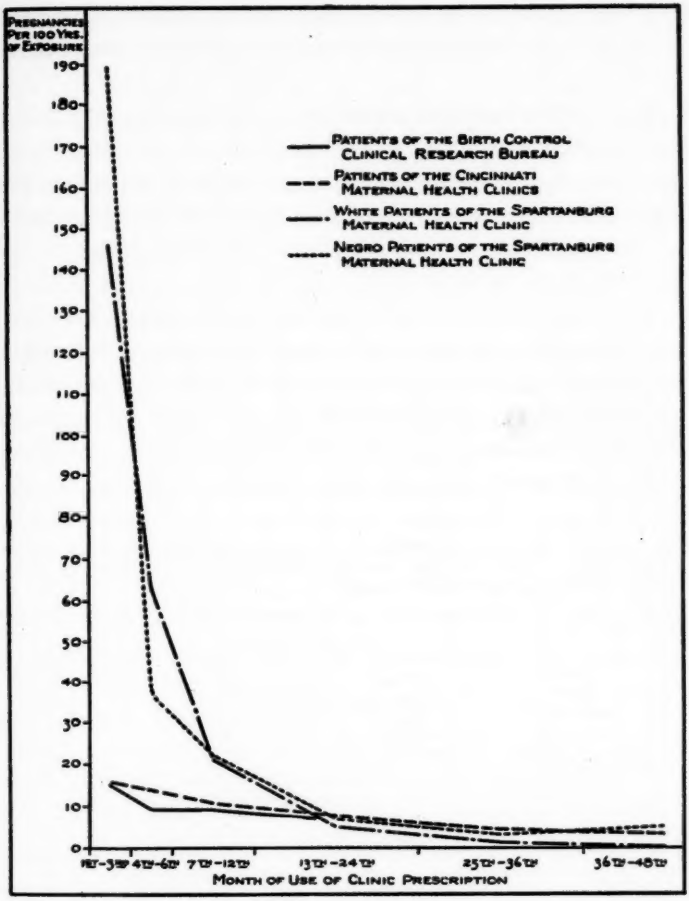

Fig. 7. Pregnancy rates in successive months of use of clinically prescribed contraceptives for four groups of women.

very low (Fig. 7). The rate for the first three months of use for Spartanburg Negro women was more than ten times as high as the corresponding rates for Cincinnati and for New York women, and the rate for white women in Spartanburg was almost as high as

that for Negroes. After fifteen months of use the rates of the Spartanburg women were as low as those of women in Cincinnati and in New York.

It is probable that the drop in rates with increasing length of use of the clinic prescription was associated with (a) an increasing dexterity in the use of the method, as the technique of use became more familiar; and (b) the fact that women who were inept in the use of the prescribed methods abandoned them and turned to other practices.

The Acceptability of the Prescribed Contraceptives. Not all women were willing to use the prescribed contraceptives, and a knowledge of the behavior of those who were unwilling to use them is as important for the formulation of effective clinic policy as is the fact that the methods prescribed were highly effective when used. Table 8 shows the proportions of women in each group of clinic

Table 8. Proportions of patients of three clinics who never used the prescribed contraceptives, who used them and then abandoned them, and who were using them at the time their records were closed.

Use of Clinic Prescription	White Patients of:			Negro Patients of Spartanburg Maternal Health Clinic
	Clinical Research Bureau (N.Y.C.)	Cincinnati Maternal Health Clinics	Spartanburg Maternal Health Clinic	
	Total number of women in need of contraception at closing date			
	943[1]	1,419[2]	412[3]	371[4]
	Per cent in each category			
Never Used	12.0	2.7	10.2	11.3
Discontinued	45.2	44.7	34.5	37.2
Using at Closing Date	42.8	52.5	55.3	51.5

[1] Total exclusive of 22 women whose exposure had ceased, and 26 women who gave up the use of CIB because they were planning pregnancy.
[2] Total exclusive of 146 women whose exposure had ceased, and 56 women ill or planning pregnancy.
[3] Total exclusive of 79 women whose postclinic experience was unknown, 2 women not fitted, 38 women whose exposure had ceased, and 2 women planning pregnancy.
[4] Total exclusive of 67 women whose postclinic experience was unknown, 18 women whose exposure had ceased, and 1 woman planning pregnancy.

patients who never used the prescribed contraceptives, who used them for a time and then discarded them, and who were using them at the time their records were closed.

The mean number of months between the initial clinic contact and the date of closing the record was about forty in Cincinnati and only about twenty in New York and in Spartanburg; therefore, the proportion of women using the prescribed contraceptives at closing date in Cincinnati is not strictly comparable with those for the other two areas. In spite of the longer average postclinic period in Cincinnati, with its correspondingly greater opportunity for loss of patients, the proportion of women using the prescribed contraceptives in any form when their records were closed was significantly higher in both Cincinnati and Spartanburg than in New York.*

The differences between the New York and Cincinnati patients were even greater when the proportions using at equal intervals following the initial clinic contact are compared. Figure 8 shows, for the four groups, the proportions of women still in need of contraception who were using the prescribed contraceptives in any form at successive intervals during the first year following their initial contact with the clinic.* In all three clinics the most rapid

*The data for all three clinics relate only to those patients who could be found and interviewed between one and five years after their initial contact with the clinic. It may be assumed that those women who failed to maintain contact with the clinics and therefore could not be found were probably not using the contraceptives prescribed for them. The possible bias introduced by the loss of between 15 and 20 per cent of the patients originally in each sample has been discussed in detail for the New York and Cincinnati clinic patients (*see* Stix and Notestein, Chapter III, pp. 92-93, Table 38; Stix, 1939, pp. 153-155, Table 14, and pp. 156-157, Table 16). In Spartanburg it was found that among the white patients lost there was a significantly higher proportion who had not reached the sixth grade than was found among those interviewed. Other differences were not significant. The lost Negro patients, on the other hand, were younger, had been married a shorter time, and had had significantly fewer pregnancies than those interviewed. Their preclinic pregnancy rates without contraception were also significantly lower than those of the interviewed patients. Among both white and Negro women the proportion of couples who had used any contraception before clinic attendance was smaller among the lost than among the interviewed patients. Thus, it may be assumed that the white patients lost were predominantly those with little or no education who had little interest in controlling their fertility, while the Negro patients lost were mainly those whose need for controlling their fertility was less than that of the women who could be found and interviewed.

*It was found in Cincinnati and Spartanburg that the proportions of patients who

(Continued on page 314)

loss of patients occurred within a brief period after the first clinic contact. At the end of one month 26 per cent of the New York patients, about 17 per cent of the Spartanburg patients, and 7 per cent of the Cincinnati patients had ceased using the prescribed contraceptives. Spartanburg white patients were slightly but not significantly more cooperative than the Negro patients. A year after they had first sought expert contraceptive advice, the proportions of women in the three areas still in need of contraception, who were using the contraceptives given them, ranged between about 55 per cent for the New York patients and for the Spartanburg Negroes and 68 per cent for the Cincinnati women. Had it been possible to compute similar figures for the lost as well as for the interviewed patients, the proportions using would have been considerably lower for all groups.

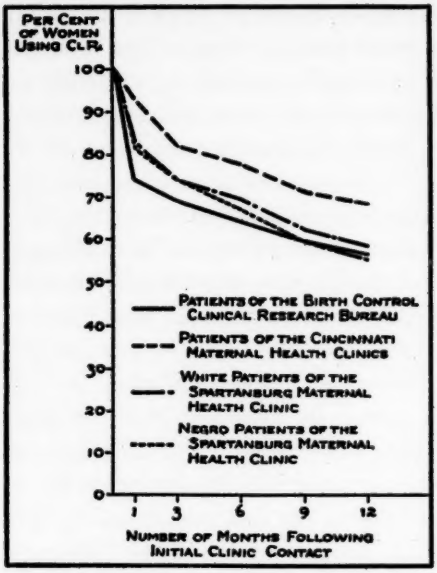

Fig. 8. Proportions of clinic patients using the prescribed contraceptives at successive intervals following their initial clinic contact.

It is probable that in New York the high immediate rate of loss and the relatively small proportion of clinic patients using the pre-

stopped using the clinic prescription were greater in the first year or two after the clinics were established than they were in later years. The proportions shown in Figure 8 are averages for the first four or five years of clinic service for these two clinics. For New York, where the clinic was well established, they are averages for the year and a half of service selected for study.

scribed contraceptives throughout the postclinic period were associated with the availability of other and more familiar types of contraception, which the New York patients found they preferred after they had given the prescribed contraceptives a trial. In Spartanburg, where cooperation with the clinic was better than in New York, but not so good as in Cincinnati, poor living conditions and general inertia operated against the consistent use of any contraceptive.

Table 9, which shows for each group of women the distribution of the reasons given for discontinuing the use of the prescribed contraceptives by those women who were dissatisfied with them,

Table 9. Distribution of reasons given for the rejection of the prescribed contraceptives by four groups of clinic patients.

Reason for Rejecting the Clinic Prescription	White Patients of:			Negro Patients of Spartanburg Maternal Health Clinic
	Clinical Research Bureau (N.Y.C.)	Cincinnati Maternal Health Clinics	Spartanburg Maternal Health Clinic	
	Number of women rejecting CIB because of dissatisfaction with it			
	539	683	184	180
	Per cent rejecting CIB for each reason			
All Reasons	100.0	100.0	100.0	100.0
Difficulty in Renewing Supplies	15.8[1]	33.5	19.6	15.0
Difficulty in Placing CIB	5.9	4.4	4.3	12.2
Discomfort for Wife or Husband	21.2	22.0	21.2	13.3
CIB Esthetically Unacceptable, or Husband Objected to its Use	13.9	11.4	7.6	12.2
CIB too much Trouble to Use	16.5	9.5	19.0	22.2
Afraid to Use CIB	13.5	4.7	7.1	3.9
Pregnant in Spite of Use	7.6	8.6	8.2	3.9
Other or Unknown	5.6	5.9	13.0	17.3

[1] Includes 57 patients who did not return because they could not pay for supplies.

throws some light on the similarities and differences in attitude in the three areas. About 20 per cent of the dissatisfied white patients in all three areas gave up the prescribed contraceptives because they were uncomfortable. The consistency of this figure should carry considerable weight with clinic administrators. Only 13 per cent of the Negro couples reported discomfort as a reason for giving up the clinic prescription, but 12 per cent reported difficulty in placing it, as compared with between 4 and 6 per cent of the white women.

About 30 per cent of all the patients prescribed for in New York City found that the clinic prescription was esthetically unacceptable, uncomfortable, difficult to place, or too much trouble to use. Corresponding proportions for white women in Spartanburg and Cincinnati were about 20 per cent and for the Negro women 24 per cent. The proportions in all three areas are too large to be ignored by clinic administrators and point to the need of prescribing other techniques for these dissatisfied patients. It is probable that in New York the large proportion of women giving up the prescribed contraceptives for these reasons did so because other and more acceptable contraceptives were easily obtainable, whereas, partly because of poverty, patients in the other two areas were compelled to lean more heavily on the clinics as their main source of supply.

The Over-All Effectiveness of Clinic Service and Its Implications for Clinic Policy

It has been shown in Table 8 that between 45 and 57 per cent of the women who sought advice from each clinic either never used the contraceptives given them or ceased using them before their records were closed. Some of these women turned to the use of other contraceptives; some abandoned the use of contraception entirely. The proportions of each type of exposure in the postclinic experience of each group are shown in Figure 9.

In New York, clinically prescribed contraceptives were used for

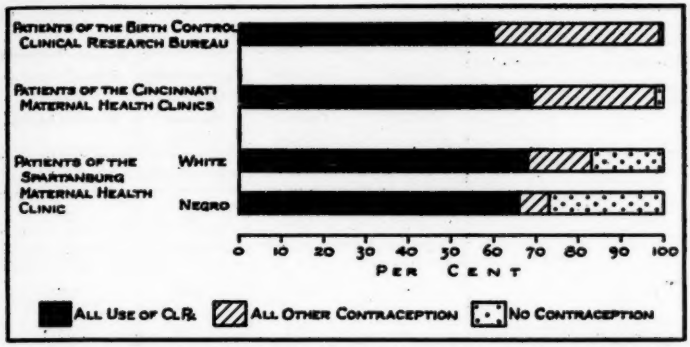
Patients of the Birth Control Clinical Research Bureau
Patients of the Cincinnati Maternal Health Clinics
Patients of the Spartanburg Maternal Health Clinic
White
Negro
0 10 20 30 40 50 60 70 80 90 100
Per Cent
All Use of C.R.
All Other Contraception
No Contraception

Fig. 9. Proportions of postclinic exposure during which four groups of clinic patients used clinic prescription, other contraceptives, and no contraception.

about 60 per cent of the total postclinic exposure, and for practically all of that remaining, other types of contraception were employed. In Cincinnati the prescribed contraceptives were used for nearly 70 per cent of the postclinic exposure, and no contraception was used for 2 per cent. In Spartanburg the clinic prescription was used for about 65 per cent of the exposure of both white and Negro women, but the proportions during which no contraception was used were 17 per cent for white and 27 per cent for Negro women.

Table 10 shows in detail the proportion of couples with each pattern of contraceptive practice after they had been advised at the clinic. The proportions using no contraception either throughout the postclinic period or after they had given up the clinic prescription were very high in Spartanburg. Thirty-nine per cent of the Negro and 23 per cent of the white women had given up any attempt to use contraception by the time their records were closed. Only 2 per cent of the women in Cincinnati and only 3 of the 991 women in New York did the same.

In New York and in Cincinnati the contraceptives most frequently used by couples who decided against using the clinic prescription were coitus interruptus and condom, in the order named (Table 11). In Spartanburg these were also the methods of choice

Contraceptive Practice after Clinic Attendance	White Patients of:			Negro Patients of Spartanburg Maternal Health Clinic
	Clinical Research Bureau (N.Y.C.)	Cincinnati Maternal Health Clinics	Spartanburg Maternal Health Clinic	
	Number of women with known postclinic exposure			
	982	1,618	448	383
	Per cent with each type of contraceptive practice			
Total	100.0	100.0	99.9	100.0
No Contraception at All	0.2	0.2	7.1	11.7
Clinic Prescription or Variant Only	40.2	51.4	56.7	50.9
Other Contraceptives Only	11.5	2.2	6.2	4.7
Clinic Prescription, Then Other Contraceptives	48.0	44.2	13.8	5.5
Clinic Prescription, Then No Contraception	0.1	2.0	16.1	27.2

Table 10. Contraceptive practice after clinic attendance for four groups of clinic patients.

of white couples but in the reverse order. Almost half of those couples who used contraceptives other than those prescribed used condoms. Fifty-six per cent of the Negro women who preferred other contraceptives to those prescribed at the clinic used douche.

All contraception was much more effective postclinic than preclinic for the patients of all three clinics. The per cent of increase in effectiveness postclinic over preclinic is shown in Figure 10. For the New York women the postclinic effectiveness of all contraceptives including those prescribed at the clinic was only 18 per cent greater than the effectiveness of all contraception before clinic attendance, because their preclinic use of contraceptives was so effective that there was little opportunity for improvement. For Cincinnati women, for whom there was greater opportunity for improvement, the increase was 63 per cent, and for Spartanburg white women 72 per cent. For the Negro women, whose preclinic contraceptive

Type of Contraception Used	White Patients of:			Negro Patients of Spartanburg Maternal Health Clinic
	Clinical Research Bureau (N.Y.C.)	Cincinnati Maternal Health Clinics	Spartanburg Maternal Health Clinic	
	Number of couples using any type of contraception except CIP or variants postclinic			
	584	750	90	39
	Per cent using each type			
Total	100.1	99.9	100.1	100.0
Condom	32.5	24.1	47.8	25.6
Coitus Interruptus	40.1	31.3	21.1	5.1
Condom or Coitus Interruptus	13.4	7.7	7.8	2.6
Douche	4.3	21.7	15.6	56.4
All Other Types[1]	9.8	15.1	7.8	10.3

[1] Includes all alternations of methods not otherwise specified, as well as suppository, sponge, jelly, etc.

Table 11. Proportion of couples, among those using contraceptives other than those prescribed, who used each contraceptive method after clinic attendance.

practice had little effect on their fertility, the increase was 179 per cent. Even when experience with the prescribed contraceptives was excluded, increases in effectiveness ranged from 15 per cent for the New York patients to 96 per cent for the Spartanburg Negroes.

There was a marked improvement in fertility control for all women who used contraception after clinic attendance, and especially for those who used clinically prescribed contraceptives. Over an extended period the fertility of the New York women could be expected to remain low, even though a large proportion of the patients abandoned the use of the prescribed contraceptives. Cincinnati patients might be expected to show a slightly greater increase in fertility than the New York women, as they turned from the clinic prescription to other types of contraception because, for this group, the postclinic effectiveness of other contraceptives was 20 per cent lower than that of the clinic prescription (Table 7). In

Spartanburg, even though other types of contraception were as effective for white women as those prescribed by the clinic, a substantial proportion of women abandoned the use of contraception and group fertility could be expected to rise as the number of these women increased. For Negro women, the increase would be even more marked because a larger proportion of them abandoned the use of contraception entirely, and the few who turned to the use of other contraceptives used mainly those that were least effective. An estimate of the rate at which group fertility might be expected to increase, as the period following the initial contact with the clinic lengthened, is shown for each of the four groups of clinic patients in Figure 11.[10] For all four groups there is a sharp drop in the number of live births per year of married life in the first year after clinic atten-

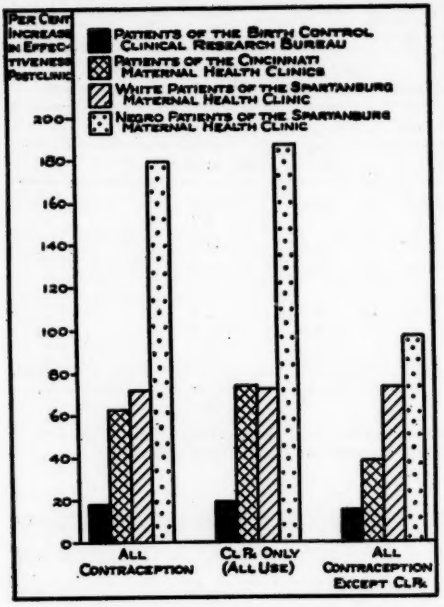

Fig. 10. Per cent of increase in the effectiveness of the contraception used after clinic attendance over that used before clinic attendance, for four groups of women.

[10] The rates (for second and later pregnancies) were derived by weighting the observed number of live births per year of married life for each type of experience by the proportions of women expected to be participating in that type of experience in each postclinic year. Rates for each type of experience were standardized to the total years-of-married-life distribution of white and Negro patients of all three clinics. The estimates for the third, fourth, and fifth years of use were made by prolonging the curves of loss of clinic patients and applying to the proportions of women abandoning the use of prescribed contraceptives in each year the observed proportions in the whole sample who turned to other contraceptives and to no contraception.

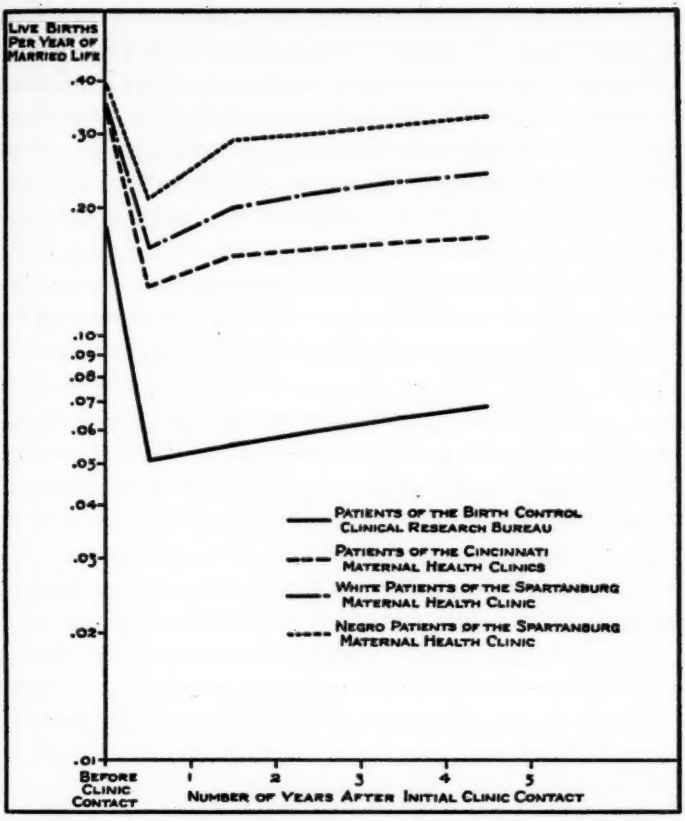

Fig. 11. Number of live births per year of married life before clinic attendance, and estimated number in successive years after clinic attendance, for four groups of women.

dance, but as more patients abandon the methods prescribed for them the fertility of each group increases. In New York the increase is negligible over an estimated five-year period. For Spartanburg Negroes, at the other extreme, the rate rises first sharply and then more gradually until in the fifth postclinic year the expected rate is very little below the preclinic rate. For the white pa-

tients in Cincinnati and Spartanburg the expected curves are intermediate between that for New York and that for the Negroes.

The trends observed in Figure 11 have important implications for clinic policy because the four groups of patients studied were typical of the widely differing groups served by physicians and clinics in various sections of the country. The New York group was probably more nearly like the patients of the average urban physician in private practice than like the patients of the other clinics under consideration. It is possible that for this group even the slight rise in fertility shown in Figure 11 might have been avoided had the patients who were dissatisfied with the clinic prescription been taught the best use of those techniques which they preferred. A detailed analysis of their reactions suggested that a more flexible policy, permitting the prescription of a wide selection of generally used techniques would probably have made for greater patient satisfaction.[12] It must be stressed repeatedly that the use of contraception involves many personal problems and adjustments, and it is important, especially for couples to whom a number of techniques are already familiar, to provide each couple with the contraceptive or contraceptives best suited to their needs and desires. A method which may be relatively ineffective for some couples may be highly effective for the couple to whom it is acceptable and who use it with care and diligence, whereas even a highly effective method is of little or no use to the couple who dislike it and will not use it consistently.

The patients of the Cincinnati clinic were probably representative of the average urban maternal-health-clinic clientele.[13] For this group also, the clinic should have offered a wider choice of contraceptive techniques and instructed the patients in the best use of those techniques. The majority of couples who discarded the clinically prescribed method turned to contraceptives they had used

[12] Stix and Notestein, Chapter XII.

[13] Stix, 1939, Foreword, to bound monograph, pp. v and vi, including footnote 4.

previously.[13] Some attempt should have been made to teach these patients how best to use the methods familiar to them. Other patients, who tried methods new to them, might have been assisted in the development of the best techniques of use of the new methods. The cost of commercial contraceptives may have prevented the use of the more effective methods, such as condom, by many couples who did not like the clinic prescription. For those couples who were not on relief, condom ranked high among alternative methods, but couples on relief depended mainly on coitus interruptus or douche.[14] Had the clinic provided other methods, such as condom, at little or no expense, the clinic service might have been considerably more effective.

The patients of the Spartanburg clinic are typical of the populations in southern areas of population pressure. The surprising finding for this group is that so many patients were willing to use a complicated contraceptive technique in spite of adverse living conditions and educational handicaps. It is probable that many women who realized the hazard of an additional pregnancy made a special effort to prevent the occurrence of such a pregnancy. Commercial methods were not readily available to them and, even if they had been, most couples had no money with which to purchase them. Thus, for indigent couples, the methods prescribed at the clinic and those which required no expenditure of money were the only ones available. The very fact that nearly half of the ninety white couples using other types of contraception postclinic used condoms (Table 11) is probably an indication that this method should have been more widely prescribed at the clinic. The Negro couples who used types of contraception other than those prescribed showed an overwhelming preference for douche after, as well as before, clinic attendance. While douche is a relatively ineffective contraceptive, its use by these Negro women after clinic attendance prevented nearly

[13] Stix, 1939, Table 21.
[14] Stix, 1939, Table 20.

60 per cent of the pregnancies that would have been expected had the same women used no contraception at all.

One problem presented by the Spartanburg patients was the wide prevalence of pathological conditions that might have been expected to interfere with the fit of a diaphragm. Thirty-five per cent of the white and 49 per cent of the Negro women had fecal impaction when they were examined at the clinic. Some of these women, as well as an additional 43 per cent of white and 33 per cent of Negro women, had cystocele or rectocele, or both. About 8 per cent more in each group could not reach the cervix because of marked obesity or short fingers. Thus, between 85 and 90 per cent of the women who came to the clinic were theoretically bad risks for diaphragm. This apparently did not affect the acceptability of the method, for there were no significant differences in the proportions of women with and without anatomical abnormalities who rejected the prescribed contraceptives, or who used them for a year or longer. The pregnancy rates of the two groups also did not differ.

It is obvious that a contraceptive service for a group such as that attending the Spartanburg Maternal Health Clinic is one which presents special problems. The ideal service for a group of such low economic and social status should offer a choice of very simple contraceptives requiring as little forethought and care as possible. The so-called "simple" feminine techniques now prescribed are cumbersome, however. For example, the Spartanburg clinician reports that few patients are willing to use sponge and foam powder because they find it uncomfortable and just as difficult to use as the diaphragm and have less confidence in it.

If patients are willing to use the diaphragm and jelly, or a similar technique, it has definite advantages over male techniques in that it puts the control of fertility into the hands of the wife, whose health is at stake. If that technique is not acceptable, however, every effort should be made to substitute another and preferable contraceptive which the couple can use effectively. The problem may be

more difficult in a rural southern area than in a city such as New York, because fewer patients will have used any contraceptives previously, and there will be less opportunity to encourage the best use of familiar techniques. The wise policy for every clinic group is to make sure that every couple is given the contraceptive or contraceptives best suited to individual needs and preferences, and to educate each patient to return to the clinic for further advice if the methods first prescribed are unsatisfactory.

The problem of including techniques other than those which up to now have had almost exclusive clinic approval, and which do not necessarily require expert fitting by a physician, may raise the question of the need of having these familiar contraceptives prescribed at a birth control clinic or by a physician. It may be assumed that expert advice on the use of any contraceptive technique may make for more effective contraceptive practice. In prescribing condoms, for example, the trained clinician can advise on the need of testing for flaws as well as on the wisdom of using a spermicide in addition to the condom. Advice may vary with patient differences in anatomy, physiology, and marital adjustment.

With the small amount of money available for subsidized contraceptive services, it would seem highly desirable that all such services be under hospital or public health supervision. Contraceptive advice should be available to all women for whom pregnancy is contraindicated, regardless of their ability to pay. To be most effective, the contraceptive clinic should be coordinated with the other services necessary for the best medical care of the patient, and should cooperate as closely as possible with referring clinics and physicians. Each patient should be encouraged to return as frequently as may be necessary, if the methods initially prescribed are not completely satisfactory.

The provision of contraceptives for the mass of the population in areas of population pressure is a matter which might well be approached differently. Subsidized services cannot possibly reach

large numbers of people, but the wider distribution of approved low-priced commercial contraceptives would probably meet the need of those people who wish to plan the size of their families but are not now able to do so satisfactorily. If such an organization as the American Medical Association would set up standards for contraceptives as it has for drugs and foods, much could be done to improve the quality of commercial contraceptives. Wise pressure on commercial distributors to bring the price of their products down to a point at which wider distribution would pay for decrease in price would probably make it possible for many people in the poorer sections of the country to purchase contraceptives not now available to them.

Even though such a program were to be instituted there would still be a residual group for whom the use of any contraceptive would be too troublesome. As Vance[25] has pointed out, a demand for contraceptives from this group will not be forthcoming until it is possible to raise the group standard of living. Thus, the solution of the problem of reducing birth rates in areas of very high fertility and low levels of living will require social changes which create and give force to a desire to limit family size.

[25] Vance, Rupert B.: The Regional Approach to the Study of High Fertility. Presented at the Round Table on Research in Factors Influencing Fertility, Nineteenth Annual Conference of the Milbank Memorial Fund, April 29-30, 1941.

ANNOTATIONS

SOCIAL AND ECONOMIC ASPECTS OF SWEDISH POPULATION MOVEMENTS, 1750-1933

DR. THOMAS' recent analysis of the social and economic aspects of Swedish population trends since 1750[1] is unique in character. The study could not be duplicated for any other country because the data do not exist.

In Sweden the continuous population register system began in the seventeenth century, for in 1686 responsibility for the registration of births, deaths, and marriages was vested in the local clergy. Today the local Swedish political unit usually coincides with the corresponding unit of the state church, the parish, and the parish registers form the basis of Swedish population and vital statistics. The records kept in each parish include the book of births and baptisms, book of deaths and burials, book of confirmations, book of banns and marriages, book of in-migrants, book of out-migrants, and book of "non-existent" (residence unknown). When a person moves from one community to another he takes with him a migration certificate which includes an abstract of his record from the previous parish. The records afford the basic materials for the periodic Swedish reports not only for birth rates, death rates, and marriage rates but also for size, distribution, and composition of the population. The keeping of a continuous "tab" on people dispenses with the necessity of our form of the decennial house-to-house census.

Fortunate for Dr. Thomas' purposes was the existence of long series of demographic data based upon the above-described records. Several decades ago Gustav Sundbärg provided from records back to 1750 a year-to-year tabulation of Sweden's population by age, sex, and marital status and computed annual rates of birth, fertility, marriage, and mor-

[1] Thomas, Dorothy S.: SOCIAL AND ECONOMIC ASPECTS OF SWEDISH POPULATION MOVEMENTS, 1750-1933. New York, The Macmillan Company, 1941, 487 pp. $6.00.

tality. These series are kept up to date in official reports. Dr. Thomas and her colleagues supplemented these series with some annual tabulations of internal migration and related factors for different types of communities for the period 1895-1933. Thanks to the work of Swedish economists and administrators, there were also available long series of data on such conditions as harvests, occupations, cost of living, wages, national income, etc.

Dr. Thomas' book is divided into two parts. The first part is devoted to the general analysis and covers the period 1750-1933. It contains, first, a factual description of population trends over the period considered, next a chapter on agricultural developments and adjustments of the agricultural population, and, finally, a chapter on industrialization in relation to population questions. The second part is focused on questions of internal migration. The detailed data on "in-migration" and "out-migration" are studied for various types of communities during the period 1895-1933.

The broad historical trends resemble those in other countries of Western civilization. The story is one of increasing urbanization and industrialization, of declining birth rates, and of the imminence of a stationary population. The unusual features of the data, however, are the possibilities for inductive study of various sorts of interrelations. The "push" and "pull" forces in population redistribution are studied by relating indices of agricultural and business prosperity to volume and direction of migration.

There are also interesting analyses of the impact of agricultural and business conditions on vital rates. During the early years of the period 1753-1913 the annual marriage rates, crude birth rates, and marital fertility rates varied directly and in a strikingly close manner with the harvest index for the preceding year. On the other hand, death rates rose after bad harvests and declined after good yields. These associations decreased in strength with the passing of time, however, and since the beginning of the present century there apparently has been only negligible impact of the harvests on vital indices.

The relation of various vital rates to business cycles was studied for the period 1865-1913. The variations in the marriage rate followed very closely those of the business cycle and this relationship persisted strongly throughout the whole period. From 1865 to 1892 there was also a high positive association between business cycles and birth and fertility rates but this was not true for the later period, 1893-1913. During neither of

these periods was the death rate found to be substantially associated with the business cycle.

Dr. Thomas discusses the declining influence of economic conditions on vital indices in the more recent periods. With respect to harvests, the development of scientific methods in agriculture has possibly reduced the magnitude of variations in crop yields. In so far as death rates are concerned, the developments in medicine and public health have probably helped to mitigate effects of vicissitudes of economic conditions. Also, increasing industrialization has meant that a declining proportion of the population is directly affected by harvests. The diminishing association between birth and fertility rates and the business cycle is a more puzzling and more complex situation. The author suggests that it "can scarcely be unconnected with the rapid downward trends in these rates, or with the differential spread of the pattern of family limitation." The situation might have been clarified somewhat if the harvest data had been related exclusively to the vital indices for the rural or agricultural population, and if the business cycle data had been related exclusively to the vital rates for the urban or non-agricultural population.

Dr. Thomas' book is replete with tables and charts, including much original data which enterprising students can doubtless use. It is fitting that the analysis of these unusual data was entrusted to one so well fitted for the job.

CLYDE V. KISER